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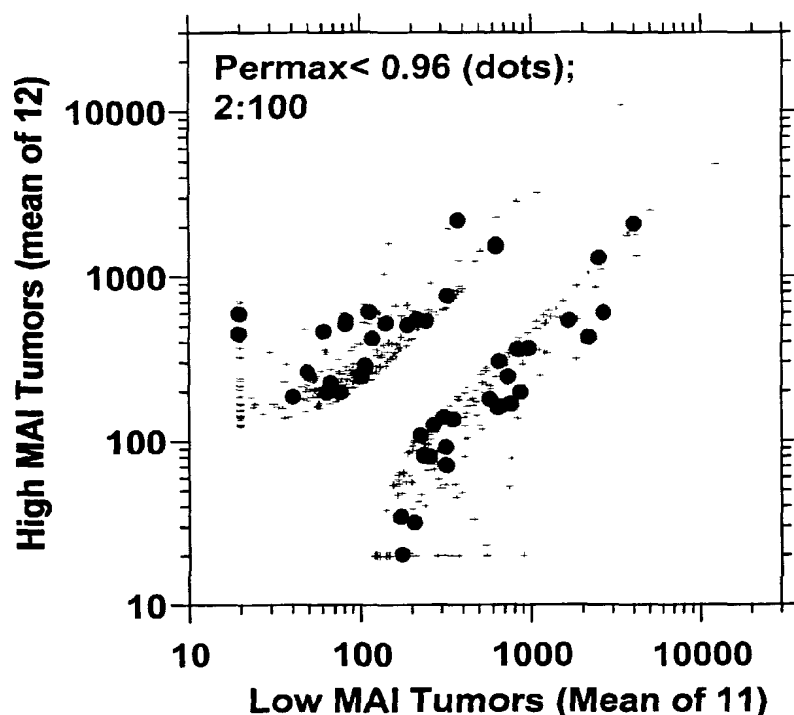
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(54) Title: PROGNOSTIC CLASSIFICATION OF BREAST CANCER



(57) Abstract: The invention provides particular sets of genes that are expressed differentially in tumors characterized as high MAI or low MAI tumors. These sets of genes can be used to discriminate between high and low MAI tumors. Diagnostic assays for classification of tumors, prediction of tumor outcome, selecting and monitoring treatment regimens and monitoring tumor progression/regression are also provided.

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PROGNOSTIC CLASSIFICATION OF BREAST CANCER

Field of the Invention

The invention relates to nucleic acid microarray markers for cancer, particularly for
5 breast cancer. The invention also relates to methods for diagnosing cancer as well as
optimizing cancer treatment strategies.

Background of the Invention

Breast cancer is a malignant proliferation of epithelial cells lining the ducts or lobules
10 of the breast (Harrison's Principles of Internal Medicine 1998). Although much progress has
been made toward understanding the biological basis of cancer and in its diagnosis and
treatment, it is still one of the leading causes of death in the United States. Inherent
difficulties in the diagnosis and treatment of cancer include among other things, the existence
of many different subgroups of cancer and the concomitant variation in appropriate treatment
15 strategies to maximize the likelihood of positive patient outcome.

The traditional method of breast cancer diagnosis and staging is through the use of
biopsy examination. Once a diagnosis is made, the options for treating breast cancer are
assessed with respect to the needs of the patient. These options traditionally include surgical
intervention, chemotherapy, radiotherapy, and adjuvant systemic therapies. Surgical therapy
20 may be lumpectomy or more extensive mastectomy. Adjuvants may include but are not
limited to chemotherapy, radiotherapy, and endocrine therapies such as castration;
administration of LHRH agonists, antiestrogens, such as tamoxifen, high-dose progestogens;
adrenalectomy; and/or aromatase inhibitors (Harrison's Principles of Internal Medicine
1998).

25 Of key importance in the treatment of breast cancer is the selection and
implementation of an appropriate combination of therapeutic approaches. For example,
depending on a breast cancer patient's prognosis, therapy may include surgical intervention
in combination with adjuvant therapy or it may only include surgical intervention. In
addition, for some patients pretreatment with chemotherapy or radiotherapy is utilized prior
30 to surgical intervention, but in other patients adjuvant therapies are used following surgical
intervention.

It is difficult to predict from standard clinical and pathologic features the clinical
course of early stage breast cancer, particularly lymph node-negative tumors in

premenopausal patients. Current practice in the United States is to offer systemic chemotherapy to most of these women. Because the majority of these women would have good outcome even without chemotherapy, the rate of “over-treatment” is high.

Chemotherapy itself carries a 1% mortality rate. Therefore, unnecessary deaths could be avoided if it were possible to subdivide these patients into high and low risk subgroups, and only undertake adjunctive treatment for those judged to be high risk.

Selection of a suitable treatment regimen for breast cancer is based on the subgroup of cancer. Current strategies used to make therapeutic decisions in the management of patients with breast cancer are based on several factors including hormone receptor status, her-2/neu staining, flow cytometry, and the mitotic activity index (MAI). The MAI is a widely utilized predictor of outcome in cancers, particularly in invasive breast cancer. The definition of the MAI is “the total number of mitoses counted in 10 consecutive high-power fields (objective, x40; numeric aperture, .75; field diameter, 450 microns), in the most cellular area at the periphery of the tumor, with the subjectively highest mitotic activity” (Jannink et al., 1995).

For the procedure, hematoxylin-eosin stained sections of breast cancer tumor are assessed for the total number of mitotic figures in ten consecutive high-power fields and based on these numbers the breast cancer is assigned to either good outcome (MAI<10) or poor outcome (MAI>10). MAI classification correlates to standard parameters such as death, recurrence, and metastases, which are known to those of ordinary skill in the art to predict clinical outcome.

Determination of appropriate treatment for an individual cancer patient is complex with a wide variety of treatments and possible treatment combinations. For example, chemotherapy is a common method of cancer treatment, with more than 50 different chemotherapeutic agents available. These therapeutic agents can be used in a wide range of dosages both singly and in combinational therapies with other chemotherapeutic agents, surgery, and/or radiotherapy.

The available methods for designing strategies for treating breast cancer patients are complex, time consuming, and inexact. The wide range of cancer subgroups and variations in disease progression limit the predictive ability of the healthcare professional. In addition, continuing development of novel treatment strategies and therapeutics will result in the addition of more variables to the already complex decision-making process involving matching the cancer patient with a treatment regimen that is appropriate and optimized for the cancer stage, extent of infiltration, tumor growth rate, and other factors central to the

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individual patient's prognosis. Because of the critical importance of selecting appropriate treatment regimens for breast cancer patients, the development of guidelines for treatment selection is of key interest to those in the medical community and their patients. Thus, there presently is a need for objective, reproducible, and sensitive methods for predicting breast cancer patient outcome and selecting optimal treatment regimens.

Summary of the Invention

It now has been discovered that particular sets of genes are expressed differentially in tumors characterized as high MAI or low MAI tumors. These sets of genes can be used to discriminate between high and low MAI tumors. Accordingly, diagnostic assays for classification of tumors, prediction of tumor outcome, selecting and monitoring treatment regimens and monitoring tumor progression/regression can now be based on the expression of sets of genes.

According to one aspect of the invention, methods for diagnosing breast cancer in a subject suspected of having breast cancer are provided. The methods include obtaining from the subject a breast tissue sample and determining the expression of a set of nucleic acid molecules or expression products thereof in the breast tissue sample. The set of nucleic acid molecules includes at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51. In preferred embodiments, the breast tissue sample suspected of being cancerous.

In some embodiments the set of nucleic acid molecules includes more than 2 and up to all of the nucleic acid molecules set forth as SEQ ID NOs:1-51, and any number of nucleic acid sequences between these two numbers. For example, in certain embodiments the set includes at least 3, 4, 5, 10, 15, 20, 30, 40 or more nucleic acid molecules of the nucleic acid molecules set forth as SEQ ID NOs:1-51.

In other embodiments, the method further includes determining the expression of the set of nucleic acid molecules or expression products thereof in a non-cancerous breast tissue sample, and comparing the expression of the set of nucleic acid molecules or expression products thereof in the breast tissue sample suspected of being cancerous and the non-cancerous breast tissue sample.

According to another aspect of the invention, methods for identifying a set of nucleic acid markers or expression products thereof are provided. The methods are effective for determining the prognosis of cancer. The methods include obtaining a plurality of tumor

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tissue samples from a plurality of subjects afflicted with cancer, classifying the plurality of tumor tissue samples according to mitotic activity index (MAI) into high MAI and low MAI groups and determining differences in the expression of a plurality of nucleic acid molecules or expression products thereof in the tumor tissue samples. The methods further include
5 selecting as a set of nucleic acid markers the nucleic acid molecules or expression products thereof which are differentially expressed in the high MAI and the low MAI groups. The set of nucleic acid markers or expression products thereof effective for determining poor prognosis of cancer includes one or more nucleic acid molecules or expression products thereof which are preferentially expressed in high MAI tumor tissue samples, and wherein the
10 set of nucleic acid markers or expression products thereof effective for determining good prognosis of cancer comprises one or more nucleic acid molecules or expression products thereof which are preferentially expressed in low MAI tumor tissue samples. In preferred embodiments, the cancer is breast cancer.

According to still another aspect of the invention, methods for selecting a course of
15 treatment of a subject having or suspected of having cancer are provided. The methods include obtaining from the subject a tissue sample suspected of being cancerous, determining the expression of a set of nucleic acid markers or expression products thereof which are differentially expressed in high MAI tumor tissue samples to determine the MAI of the tissue sample of the subject, and selecting a course of treatment appropriate to the cancer of the
20 subject.

In preferred embodiments the cancer is breast cancer, and in some of these embodiments the methods include determining the expression of a set of nucleic acid markers that are differentially expressed in low MAI breast tumor tissue samples.

According to yet another aspect of the invention, methods for evaluating treatment of
25 cancer are provided. The methods include obtaining a first determination of the expression of a set of nucleic acid molecules or expression products thereof, which are differentially expressed in high MAI tumor tissue samples to determine the MAI of the tissue sample from a subject undergoing treatment for cancer, and obtaining a second determination of the expression of a set of nucleic acid molecules or expression products thereof, which are
30 differentially expressed in high MAI tumor tissue samples to determine the MAI of the second tissue sample from the subject after obtaining the first determination. The methods also include comparing the first determination of expression to the second determination of expression as an indication of evaluation of the treatment.

In preferred embodiments the cancer is breast cancer, and in some of these embodiments the methods include determining the expression of a set of nucleic acid markers that are differentially expressed in low MAI breast tumor tissue samples.

The invention in another aspect provides solid-phase nucleic acid molecule arrays.

5 The arrays have a cancer gene marker set that consists essentially of at least two and as many as all of the nucleic acid molecules set forth as SEQ ID NOs:1-51 fixed to a solid substrate. The set of nucleic acid markers can include any number of nucleic acid sequences between these two numbers, selected from SEQ ID NOs:1-51. For example, in certain embodiments the set includes at least 3, 4, 5, 10, 15, 20, 30, 40 or more nucleic acid molecules of the
10 nucleic acid molecules set forth as SEQ ID NOs:1-51. In some embodiments, the solid-phase nucleic acid molecule array also includes at least one control nucleic acid molecule.

In certain embodiments, the solid substrate includes a material selected from the group consisting of glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon. Preferably the substrate is glass.

15 In other embodiments, the nucleic acid molecules are fixed to the solid substrate by covalent bonding.

According to yet another aspect of the invention, protein microarrays are provided.

The protein microarrays include antibodies or antigen-binding fragments thereof, that specifically bind at least two different polypeptides selected from the group consisting of
20 SEQ ID NOs:52-102, fixed to a solid substrate. In some embodiments, the microarray comprises antibodies or antigen-binding fragments thereof, that bind specifically to least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50 or 51 different polypeptides selected from the group consisting of SEQ ID NOs:52-102. In certain
25 embodiments, the microarray also includes an antibody or antigen-binding fragment thereof, that binds specifically to a cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs:52-102, preferably a breast cancer associated polypeptide. In some embodiments, the protein microarray also includes at least one control polypeptide molecule. In further embodiments, the antibodies are monoclonal or polyclonal antibodies.
30 In other embodiments, the antibodies are chimeric, human, or humanized antibodies. In some embodiments, the antibodies are single chain antibodies. In still other embodiments, the antigen-binding fragments are F(ab')₂, Fab, Fd, or Fv fragments.

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In a further aspect of the invention, methods for identifying lead compounds for a pharmacological agent useful in the treatment of breast cancer are provided. The methods include contacting a breast cancer cell or tissue with a candidate pharmacological agent, and determining the expression of a set of nucleic acid molecules in the breast cancer cell or
5 tissue sample under conditions which, in the absence of the candidate pharmacological agent, permit a first amount of expression of the set of nucleic acid molecules. The set of nucleic acid molecules includes at least two and as many as all of the nucleic acid molecules set forth as SEQ ID NOs:1-51. The methods also include detecting a test amount of the expression of the set of nucleic acid molecules, wherein a decrease in the test amount of expression in the
10 presence of the candidate pharmacological agent relative to the first amount of expression indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which is useful in the treatment of breast cancer. In preferred embodiments, the set of nucleic acid molecules is differentially expressed in high MAI breast tumor tissue samples.

In some embodiments of any of the foregoing methods and products, the differences
15 in the expression of a the nucleic acid molecules are determined by nucleic acid hybridization or nucleic acid amplification methods. Preferably the nucleic acid hybridization is performed using a solid-phase nucleic acid molecule array. In other embodiments, the differences in the expression of the nucleic acid molecules are determined by protein expression analysis, preferably SELDI mass spectroscopy.

20 These and other aspects of the invention will be described in greater detail below.

Brief Description of the Drawings

Figure 1 is a scatterplot of gene expression level in low risk (x axis) and high risk (y axis) breast cancers. 422 genes whose mean expression between groups differs at least 2-fold
25 and by 100 expression units are shown as small crosses. The top 51 t-test ranked genes with $\text{Permax} = 0.96$ are indicated as solid circles, and appear in Table 1.

Detailed Description of the Invention

The invention described herein relates to the identification of a set of genes expressed
30 in breast cancer tissue that are predictive of the clinical outcome of the cancer. Changes in cell phenotype in cancer are often the result of one or more changes in the genome expression of the cell. Some genes are expressed in tumor cells, and not in normal cells. In addition, different genes are expressed in different subgroups of breast cancers, which have different

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prognoses and require different treatment regimens to optimize patient outcome. The differential expression of breast cancer genes can be examined by the assessment of nucleic acid or protein expression in the breast cancer tissue.

The genes were identified by screening nucleic acid molecules isolated from various breast cancer samples for expression of the genes present on a high-density nucleic acid microarray. The breast cancer samples were categorized with respect to their mitotic activity index (MAI) and the MAI was correlated to gene expression to identify those genes differentially expressed between low and high-MAI breast cancer tissue. The MAI has been shown to correlate with the outcome of the cancer as defined by tumor metastasis, tumor recurrence or mortality. Accordingly the genes identified permit, *inter alia*, rapid screening of cancer samples by nucleic acid microarray hybridization or protein expression technology to determine the expression of the specific genes and thereby to predict the outcome of the cancer. Such screening is beneficial, for example, in selecting the course of treatment to provide to the cancer patient, and to monitor the efficacy of a treatment.

The invention differs from traditional breast cancer diagnostic and classification techniques including MAI, hormone receptor expression and her-2/neu expression, with respect to the speed, simplicity, and reproducibility of the cancer diagnostic assay. The invention also presents targets for drug development because it identifies genes that are differentially expressed in poor outcome breast tumors, which can be utilized in the development of drugs to treat such tumors, e.g., by reducing expression of the genes or reducing activity of proteins encoded by the genes.

The invention moves beyond the use of the MAI and simplifies prognosis determination by providing an identified set of genes whose expression in breast cancers predicts poor clinical outcome as defined by tumor metastasis, recurrence, or death. In the invention, the MAI was used in conjunction with RNA expression phenotyping performed using high density microarrays generated from quantitative expression data on over 5000 (estimated 5800) genes, which have been analyzed to identify 51 specific probe sets (genes) with divergent expression between MAI groups. The expression gene set has multifold uses including, but not limited to, the following examples. The expression gene set may be used as a prognostic tool for breast cancer patients, to make possible more finely tuned diagnosis of breast cancer and allow healthcare professionals to tailor treatment to individual patients' needs. The invention can also assess the efficacy of breast cancer treatment by determining progression or regression of breast cancer in patients before, during, and after breast cancer

treatment. Another utility of the expression gene set is in the biotechnology and pharmaceutical industries' research on disease pathway discovery for therapeutic targeting. The invention can identify alterations in gene expression in breast cancer and can also be used to uncover and test candidate pharmaceutical agents to treat breast cancer.

5 Although the invention is described primarily with respect to breast cancer, one of ordinary skill in the art will appreciate that the invention also is useful for diagnosis and prognosis determination of cancers that can be classified into subgroups for prognosis of the cancer based on MAI. For example, MAI has been used successfully in the classification of malignant melanoma, ovarian cancer, bladder cancer, and prostatic adenocarcinoma. Thus,
10 the methods and products of the invention also are applicable to non-breast cancers that can be classified by MAI.

 The invention may also encompass cancers other than breast cancer, including but not limited to: biliary tract cancer; bladder cancer; brain cancer including glioblastomas and medulloblastomas; cervical cancer; choriocarcinoma; colon cancer; endometrial cancer;
15 esophageal cancer; gastric cancer; hematological neoplasms including acute lymphocytic and myelogenous leukemia; multiple myeloma; AIDS-associated leukemias and adult T-cell leukemia lymphoma; intraepithelial neoplasms including Bowen's disease and Paget's disease; liver cancer; lung cancer; lymphomas including Hodgkin's disease and lymphocytic lymphomas; neuroblastomas; oral cancer including squamous cell carcinoma; ovarian cancer
20 including those arising from epithelial cells, stromal cells, germ cells and mesenchymal cells; pancreatic cancer; prostate cancer; rectal cancer; sarcomas including leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma, and osteosarcoma; skin cancer including melanoma, Kaposi's sarcoma, basocellular cancer, and squamous cell cancer; testicular cancer including germinal tumors such as seminoma, non-seminoma (teratomas,
25 choriocarcinomas), stromal tumors, and germ cell tumors; thyroid cancer including thyroid adenocarcinoma and medullar carcinoma; and renal cancer including adenocarcinoma and Wilms tumor.

 As used herein, a subject is a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat or rodent. In all embodiments human subjects are preferred. Preferably the
30 subject is a human either suspected of having breast cancer, or having been diagnosed with breast cancer. In a preferred embodiment of the invention the cancer is pre-menopausal, lymph node-negative breast cancer. Methods for identifying subjects suspected of having breast cancer may include manual examination, biopsy, subject's family medical history,

subject's medical history, or a number of imaging technologies such as mammography, magnetic resonance imaging, magnetic resonance spectroscopy, or positron emission tomography. Diagnostic methods for breast cancer and the clinical delineation of breast cancer diagnoses are well-known to those of skill in the medical arts.

5 As used herein, breast tissue sample is tissue obtained from a breast tissue biopsy using methods well-known to those of ordinary skill in the related medical arts. The phrase "suspected of being cancerous" as used herein means a breast cancer tissue sample believed by one of ordinary skill in the medical arts to contain cancerous cells. Methods for obtaining the sample from the biopsy include gross apportioning of a mass, microdissection, laser-
10 based microdissection, or other art-known cell-separation methods.

Because of the variability of the cell types in diseased-tissue biopsy material, and the variability in sensitivity of the diagnostic methods used, the sample size required for analysis may range from 1, 10, 50, 100, 200, 300, 500, 1000, 5000, 10,000, to 50,000 or more cells. The appropriate sample size may be determined based on the cellular composition and
15 condition of the biopsy and the standard preparative steps for this determination and subsequent isolation of the nucleic acid for use in the invention are well known to one of ordinary skill in the art. An example of this, although not intended to be limiting, is that in some instances a sample from the biopsy may be sufficient for assessment of RNA expression without amplification, but in other instances the lack of suitable cells in a small
20 biopsy region may require use of RNA conversion and/or amplification methods or other methods to enhance resolution of the nucleic acid molecules. Such methods, which allow use of limited biopsy materials, are well known to those of ordinary skill in the art and include, but are not limited to: direct RNA amplification, reverse transcription of RNA to cDNA, amplification of cDNA, or the generation of radio-labeled nucleic acids.

25 As used herein, the phrase "determining the expression of a set of nucleic acid molecules in the breast tissue" means identifying RNA transcripts in the tissue sample by analysis of nucleic acid or protein expression in the tissue sample. As used herein, "set" refers to a group of nucleic acid molecules that include 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39,
30 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, or 51 different nucleic acid sequences from the group of nucleic acid sequences numbered 1 through 51 in Table 1 (SEQ ID Nos: 1-51).

The expression of the set of nucleic acid molecules in the sample from the breast cancer patient can be compared to the expression of the set of nucleic acid molecules in a

sample of breast tissue that is non-cancerous. As used herein, non-cancerous breast tissue means tissue determined by one of ordinary skill in the medical art to have no evidence of breast cancer based on standard diagnostic methods including, but not limited to, histologic staining and microscopic analysis.

5 Nucleic acid markers for cancer are nucleic acid molecules that by their presence or absence indicate the presence or absence of breast cancer. In tissue, certain nucleic acid molecules are expressed at different levels depending on whether tissue is non-cancerous or cancerous. In cancerous tissue, nucleic acid molecule expression may be correlated with MAI prognostic analysis. As described herein, breast cancer nucleic acid markers were
10 identified by evaluating the nucleic acid molecules present in breast tumor tissue samples and comparing expression levels of the nucleic acid molecules with MAI levels determined for the tissues. An aspect of the invention is that different nucleic acid molecules are expressed in breast cancers with different MAI levels (i.e., high MAI versus low MAI) and these expression variations are identifiable by nucleic acid expression analysis, such as microarray
15 analysis or protein expression analysis. Some nucleic acids are more likely to be, in other words, are preferentially expressed in cancers with high MAI levels and other nucleic acids are preferentially expressed in cancers with low MAI levels. According to the invention, the correlation between the preferential expression of nucleic acid markers and MAI classification allows expression of nucleic acid markers to be used to directly categorize
20 breast cancers as low MAI or high MAI. Thus, nucleic acid expression-based categorization of breast cancer (by measurement of nucleic acid or protein expression) as low or high MAI may be used by one of ordinary skill in the medical arts to select an appropriate treatment regimen based on a patient's specific breast cancer prognosis.

Hybridization methods for nucleic acids are well known to those of ordinary skill in
25 the art (see, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York). The nucleic acid molecules from a breast cancer tissue sample hybridize under stringent conditions to nucleic acid markers expressed in breast cancer. In one embodiment
30 the markers are sets of two or more of the nucleic acid molecules as set forth in SEQ ID NOs: 1 through 51.

The breast cancer nucleic acid markers disclosed herein are known genes and fragments thereof. It may be desirable to identify variants of those genes, such as allelic

variants or single nucleotide polymorphisms (SNPs) in tissues. Accordingly, methods for identifying breast cancer nucleic acid markers, including variants of the disclosed full-length cDNAs, genomic DNAs, and SNPs are also included in the invention. The methods include contacting a nucleic acid sample (such as a cDNA library, genomic library, genomic DNA isolate, etc.) with a nucleic acid probe or primer derived from one of SEQ ID NOs:1 through 51. The nucleic acid sample and the probe or primer hybridize to complementary nucleotide sequences of nucleic acids in the sample, if any are present, allowing detection of nucleic acids related to SEQ ID NOs: 1-51. Preferably the probe or primer is detectably labeled. The specific conditions, reagents, and the like can be selected by one of ordinary skill in the art to selectively identify nucleic acids related to sets of two or more of SEQ ID NOs:1 through 51. The isolated nucleic acid molecule can be sequenced according to standard procedures.

In addition to native nucleic acid markers (SEQ ID NOs:1-51), the invention also includes degenerate nucleic acids that include alternative codons to those present in the native materials. For example, serine residues are encoded by the codons TCA, AGT, TCC, TCG, TCT, and AGC. Each of the six codons is equivalent for the purposes of encoding a serine residue. Similarly, nucleotide sequence triplets that encode other amino acid residues include, but are not limited to: CCA, CCC, CCG, and CCT (proline codons); CGA, CGC, CGG, CGT, AGA, and AGG (arginine codons); ACA, ACC, ACG, and ACT (threonine codons); AAC and AAT (asparagine codons); and ATA, ATC, and ATT (isoleucine codons). Other amino acid residues may be encoded similarly by multiple nucleotide sequences. Thus, the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code.

The invention also provides modified nucleic acid molecules, which include additions, substitutions, and deletions of one or more nucleotides such as the allelic variants and SNPs described above. In preferred embodiments, these modified nucleic acid molecules and/or the polypeptides they encode retain at least one activity or function of the unmodified nucleic acid molecule and/or the polypeptides, such as hybridization, antibody binding, etc. In certain embodiments, the modified nucleic acid molecules encode modified polypeptides, preferably polypeptides having conservative amino acid substitutions. As used herein, a “conservative amino acid substitution” refers to an amino acid substitution which does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Conservative substitutions of amino acids include substitutions made amongst amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H;

(d) A, G; (e) S, T; (f) Q, N; and (g) E, D. The modified nucleic acid molecules are structurally related to the unmodified nucleic acid molecules and in preferred embodiments are sufficiently structurally related to the unmodified nucleic acid molecules so that the modified and unmodified nucleic acid molecules hybridize under stringent conditions known to one of skill in the art.

For example, modified nucleic acid molecules that encode polypeptides having single amino acid changes can be prepared for use in the methods and products disclosed herein. Each of these nucleic acid molecules can have one, two, or three nucleotide substitutions exclusive of nucleotide changes corresponding to the degeneracy of the genetic code as described herein. Likewise, modified nucleic acid molecules that encode polypeptides having two amino acid changes can be prepared, which have, e.g., 2-6 nucleotide changes. Numerous modified nucleic acid molecules like these will be readily envisioned by one of skill in the art, including for example, substitutions of nucleotides in codons encoding amino acids 2 and 3, 2 and 4, 2 and 5, 2 and 6, and so on. In the foregoing example, each combination of two amino acids is included in the set of modified nucleic acid molecules, as well as all nucleotide substitutions which code for the amino acid substitutions. Additional nucleic acid molecules that encode polypeptides having additional substitutions (i.e., 3 or more), additions or deletions [e.g., by introduction of a stop codon or a splice site(s)] also can be prepared and are embraced by the invention as readily envisioned by one of ordinary skill in the art. Any of the foregoing nucleic acids can be tested by routine experimentation for retention of structural relation to or activity similar to the nucleic acids disclosed herein.

In the invention, standard hybridization techniques of microarray technology are utilized to assess patterns of nucleic acid expression and identify nucleic acid marker expression. Microarray technology, which is also known by other names including: DNA chip technology, gene chip technology, and solid-phase nucleic acid array technology, is well known to those of ordinary skill in the art and is based on, but not limited to, obtaining an array of identified nucleic acid probes on a fixed substrate, labeling target molecules with reporter molecules (e.g., radioactive, chemiluminescent, or fluorescent tags such as fluorescein, Cy3-dUTP, or Cy5-dUTP), hybridizing target nucleic acids to the probes, and evaluating target-probe hybridization. A probe with a nucleic acid sequence that perfectly matches the target sequence will, in general, result in detection of a stronger reporter-molecule signal than will probes with less perfect matches. Many components and techniques utilized in nucleic acid microarray technology are presented in *The Chipping*

Forecast, Nature Genetics, Vol.21, Jan 1999, the entire contents of which is incorporated by reference herein.

According to the present invention, microarray substrates may include but are not limited to glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon. In all embodiments a glass substrate is preferred. According to the invention, probes are selected from the group of nucleic acids including, but not limited to: DNA, genomic DNA, cDNA, and oligonucleotides; and may be natural or synthetic. Oligonucleotide probes preferably are 20 to 25-mer oligonucleotides and DNA/cDNA probes preferably are 500 to 5000 bases in length, although other lengths may be used. Appropriate probe length may be determined by one of ordinary skill in the art by following art-known procedures. In one embodiment, preferred probes are sets of two or more of the nucleic acid molecules set forth as SEQ ID NO: 1 through 51 (see also Table 1). Probes may be purified to remove contaminants using standard methods known to those of ordinary skill in the art such as gel filtration or precipitation.

In one embodiment, the microarray substrate may be coated with a compound to enhance synthesis of the probe on the substrate. Such compounds include, but are not limited to, oligoethylene glycols. In another embodiment, coupling agents or groups on the substrate can be used to covalently link the first nucleotide or oligonucleotide to the substrate. These agents or groups may include, but are not limited to: amino, hydroxy, bromo, and carboxy groups. These reactive groups are preferably attached to the substrate through a hydrocarbyl radical such as an alkylene or phenylene divalent radical, one valence position occupied by the chain bonding and the remaining attached to the reactive groups. These hydrocarbyl groups may contain up to about ten carbon atoms, preferably up to about six carbon atoms. Alkylene radicals are usually preferred containing two to four carbon atoms in the principal chain. These and additional details of the process are disclosed, for example, in U.S. Patent 4,458,066, which is incorporated by reference in its entirety.

In one embodiment, probes are synthesized directly on the substrate in a predetermined grid pattern using methods such as light-directed chemical synthesis, photochemical deprotection, or delivery of nucleotide precursors to the substrate and subsequent probe production.

In another embodiment, the substrate may be coated with a compound to enhance binding of the probe to the substrate. Such compounds include, but are not limited to: polylysine, amino silanes, amino-reactive silanes (Chipping Forecast, 1999) or chromium

(Gwynne and Page, 2000). In this embodiment, presynthesized probes are applied to the substrate in a precise, predetermined volume and grid pattern, utilizing a computer-controlled robot to apply probe to the substrate in a contact-printing manner or in a non-contact manner such as ink jet or piezo-electric delivery. Probes may be covalently linked to the substrate with methods that include, but are not limited to, UV-irradiation. In another embodiment probes are linked to the substrate with heat.

Targets are nucleic acids selected from the group, including but not limited to: DNA, genomic DNA, cDNA, RNA, mRNA and may be natural or synthetic. In all embodiments, nucleic acid molecules from human breast tissue are preferred. The tissue may be obtained from a subject or may be grown in culture (e.g. from a breast cancer cell line).

In embodiments of the invention one or more control nucleic acid molecules are attached to the substrate. Preferably, control nucleic acid molecules allow determination of factors including but not limited to: nucleic acid quality and binding characteristics; reagent quality and effectiveness; hybridization success; and analysis thresholds and success. Control nucleic acids may include but are not limited to expression products of genes such as housekeeping genes or fragments thereof.

To select a set of tumor markers, the expression data generated by, for example, microarray analysis of gene expression, is preferably analyzed to determine which genes in different groups of cancer tissues are significantly differentially expressed. In the methods disclosed herein, the significance of gene expression was determined using Permax computer software, although any standard statistical package that can discriminate significant differences in expression may be used. Permax performs permutation 2-sample t-tests on large arrays of data. For high dimensional vectors of observations, the Permax software computes t-statistics for each attribute, and assesses significance using the permutation distribution of the maximum and minimum overall attributes. The main use is to determine the attributes (genes) that are the most different between two groups (e.g., high MAI tissues versus low MAI tissues), measuring "most different" using the value of the t-statistics, and their significance levels.

In one embodiment of the invention, expression of nucleic acid markers is used to select clinical treatment paradigms for breast cancer. Treatment options, as described herein, may include but are not limited to: chemotherapy, radiotherapy, adjuvant therapy, or any combination of the aforementioned methods. Aspects of treatment that may vary include, but are not limited to: dosages, timing of administration, or duration of therapy; and may or may

not be combined with other treatments, which may also vary in dosage, timing, or duration. Another treatment for breast cancer is surgery, which can be utilized either alone or in combination with any of the aforementioned treatment methods. One of ordinary skill in the medical arts may determine an appropriate treatment paradigm based on evaluation of differential expression of sets of two or more of the nucleic acid targets SEQ ID NOs:1-51. Cancers that express markers that are indicative of a more aggressive cancer or poor prognosis may be treated with more aggressive therapies.

Progression or regression of breast cancer is determined by comparison of two or more different breast cancer tissue samples taken at two or more different times from a subject. For example, progression or regression may be evaluated by assessments of expression of sets of two or more of the nucleic acid targets, including but not limited to SEQ ID NOs:1-51, in a breast cancer tissue sample from a subject before, during, and following treatment for breast cancer.

In another embodiment, novel pharmacological agents useful in the treatment of breast cancer can be identified by assessing variations in the expression of sets of two or more breast cancer nucleic acid markers, from among SEQ ID NOs:1-51, prior to and after contacting breast cancer cells or tissues with candidate pharmacological agents for the treatment of breast cancer. The cells may be grown in culture (e.g. from a breast cancer cell line), or may be obtained from a subject, (e.g. in a clinical trial of candidate pharmaceutical agents to treat breast cancer). Alterations in expression of two or more sets of breast cancer nucleic acid markers, from among SEQ ID NOs:1-51, in breast cancer cells or tissues tested before and after contact with a candidate pharmacological agent to treat breast cancer, indicate progression, regression, or stasis of the breast cancer thereby indicating efficacy of candidate agents and concomitant identification of lead compounds for therapeutic use in breast cancer.

The invention further provides efficient methods of identifying pharmacological agents or lead compounds for agents active at the level of breast cancer cellular function. Generally, the screening methods involve assaying for compounds that beneficially alter breast cancer nucleic acid molecule expression. Such methods are adaptable to automated, high throughput screening of compounds.

The assay mixture comprises a candidate pharmacological agent. Typically, a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a different response to the various concentrations. Typically, one of these concentrations

serves as a negative control, i.e., at zero concentration of agent or at a concentration of agent below the limits of assay detection. Candidate agents encompass numerous chemical classes, although typically they are organic compounds. Preferably, the candidate pharmacological agents are small organic compounds, i.e., those having a molecular weight of more than 50 yet less than about 2500, preferably less than about 1000 and, more preferably, less than about 500. Candidate agents comprise functional chemical groups necessary for structural interactions with polypeptides and/or nucleic acids, and typically include at least an amine, carbonyl, hydroxyl or carboxyl group, preferably at least two of the functional chemical groups and more preferably at least three of the functional chemical groups. The candidate agents can comprise cyclic carbon or heterocyclic structure and/or aromatic or polyaromatic structures substituted with one or more of the above-identified functional groups. Candidate agents also can be biomolecules such as peptides, saccharides, fatty acids, sterols, isoprenoids, purines, pyrimidines, derivatives or structural analogs of the above, or combinations thereof and the like. Where the agent is a nucleic acid, the agent typically is a DNA or RNA molecule, although modified nucleic acids as defined herein are also contemplated.

Candidate agents are obtained from a wide variety of sources including libraries of synthetic or natural compounds. For example, numerous means are available for random and directed synthesis of a wide variety of organic compounds and biomolecules, including expression of randomized oligonucleotides, synthetic organic combinatorial libraries, phage display libraries of random peptides, and the like. Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant and animal extracts are available or readily produced. Additionally, natural and synthetically produced libraries and compounds can be readily be modified through conventional chemical, physical, and biochemical means. Further, known pharmacological agents may be subjected to directed or random chemical modifications such as acylation, alkylation, esterification, amidification, etc. to produce structural analogs of the agents.

A variety of other reagents also can be included in the mixture. These include reagents such as salts, buffers, neutral proteins (e.g., albumin), detergents, etc. which may be used to facilitate optimal protein-protein and/or protein-nucleic acid binding. Such a reagent may also reduce non-specific or background interactions of the reaction components. Other reagents that improve the efficiency of the assay such as protease, inhibitors, nuclease inhibitors, antimicrobial agents, and the like may also be used.

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The mixture of the foregoing assay materials is incubated under conditions whereby, the anti-breast cancer candidate agent specifically binds the cellular binding target, a portion thereof or analog thereof. The order of addition of components, incubation temperature, time of incubation, and other parameters of the assay may be readily determined. Such
5 experimentation merely involves optimization of the assay parameters, not the fundamental composition of the assay. Incubation temperatures typically are between 4°C and 40°C. Incubation times preferably are minimized to facilitate rapid, high throughput screening, and typically are between 0.1 and 10 hours.

After incubation, the presence or absence of specific binding between the anti-breast
10 cancer candidate agent and one or more binding targets is detected by any convenient method available to the user. For cell-free binding type assays, a separation step is often used to separate bound from unbound components. The separation step may be accomplished in a variety of ways. Conveniently, at least one of the components is immobilized on a solid substrate, from which the unbound components may be easily separated. The solid substrate
15 can be made of a wide variety of materials and in a wide variety of shapes, e.g., microtiter plate, microbead, dipstick, resin particle, etc. The substrate preferably is chosen to maximize signal to noise ratios, primarily to minimize background binding, as well as for ease of separation and cost.

Separation may be effected for example, by removing a bead or dipstick from a
20 reservoir, emptying or diluting a reservoir such as a microtiter plate well, rinsing a bead, particle, chromatographic column or filter with a wash solution or solvent. The separation step preferably includes multiple rinses or washes. For example, when the solid substrate is a microtiter plate, the wells may be washed several times with a washing solution, which typically includes those components of the incubation mixture that do not participate in
25 specific bindings such as salts, buffer, detergent, non-specific protein, etc. Where the solid substrate is a magnetic bead, the beads may be washed one or more times with a washing solution and isolated using a magnet.

Detection may be effected in any convenient way for cell-based assays such as two- or three-hybrid screens. The transcript resulting from a reporter gene transcription assay of
30 the anti-cancer agent binding to a target molecule typically encodes a directly or indirectly detectable product, e.g., β -galactosidase activity, luciferase activity, and the like. For cell-free binding assays, one of the components usually comprises, or is coupled to, a detectable label. A wide variety of labels can be used, such as those that provide direct detection (e.g.,

radioactivity, luminescence, optical or electron density, etc). or indirect detection (e.g., epitope tag such as the FLAG epitope, enzyme tag such as horseshoe peroxidase, etc.). The label may be bound to an anti-cancer agent binding partner, or incorporated into the structure of the binding partner.

5 A variety of methods may be used to detect the label, depending on the nature of the label and other assay components. For example, the label may be detected while bound to the solid substrate or subsequent to separation from the solid substrate. Labels may be directly detected through optical or electron density, radioactive emissions, nonradiative energy transfers, etc. or indirectly detected with antibody conjugates, streptavidin-biotin conjugates,
10 etc. Methods for detecting the labels are well known in the art.

 The invention provides breast cancer gene-specific binding agents, methods of identifying and making such agents, and their use in diagnosis, therapy and pharmaceutical development. For example, breast cancer gene-specific pharmacological agents are useful in a variety of diagnostic and therapeutic applications as described herein. In general, the
15 specificity of a breast cancer gene binding to a binding agent is shown by binding equilibrium constants. Targets which are capable of selectively binding a breast cancer gene preferably have binding equilibrium constants of at least about 10^7 M^{-1} , more preferably at least about 10^8 M^{-1} , and most preferably at least about 10^9 M^{-1} . The wide variety of cell based and cell
20 free assays may be used to demonstrate breast cancer gene-specific binding. Cell-based assays include one, two and three hybrid screens, assays in which breast cancer gene-mediated transcription is inhibited or increased, etc. Cell-free assays include breast cancer gene-protein binding assays, immunoassays, etc. Other assays useful for screening agents which bind breast cancer polypeptides include fluorescence resonance energy transfer (FRET), and electrophoretic mobility shift analysis (EMSA).

25 In another aspect of the invention, pre- and post-treatment alterations in expression of two or more sets of breast cancer nucleic acid markers including, but not limited to, SEQ ID NOs:1-51 in breast cancer cells or tissues may be used to assess treatment parameters including, but not limited to: dosage, method of administration, timing of administration, and combination with other treatments as described herein.

30 Candidate pharmacological agents may include antisense oligonucleotides that selectively binds to a breast cancer nucleic acid marker molecule, as identified herein, to reduce the expression of the marker molecules in breast cancer cells and tissues. One of ordinary skill in the art can test of the effects of a reduction of expression of breast cancer

nucleic acid marker sequences *in vivo* or *in vitro*, to determine the efficacy of one or more antisense oligonucleotides.

As used herein, the term “antisense oligonucleotide” or “antisense” describes an oligonucleotide that is an oligoribonucleotide, oligodeoxyribonucleotide, modified
5 oligoribonucleotide, or modified oligodeoxyribonucleotide which hybridizes under physiological conditions to DNA comprising a particular gene or to an mRNA transcript of that gene and, thereby, inhibits the transcription of that gene and/or the translation of that mRNA. The antisense molecules are designed so as to interfere with transcription or translation of a target gene upon hybridization with the target gene or transcript. Those
10 skilled in the art will recognize that the exact length of the antisense oligonucleotide and its degree of complementarity with its target will depend upon the specific target selected, including the sequence of the target and the particular bases which comprise that sequence. It is preferred that the antisense oligonucleotide be constructed and arranged so as to bind selectively with the target under physiological conditions, i.e., to hybridize substantially more
15 to the target sequence than to any other sequence in the target cell under physiological conditions.

Based upon the sequences of breast cancer expressed nucleic acids, or upon allelic or homologous genomic and/or cDNA sequences, one of skill in the art can easily choose and synthesize any of a number of appropriate antisense molecules for use in accordance with the
20 present invention. In order to be sufficiently selective and potent for inhibition, such antisense oligonucleotides should comprise at least 10 and, more preferably, at least 15 consecutive bases that are complementary to the target, although in certain cases modified oligonucleotides as short as 7 bases in length have been used successfully as antisense oligonucleotides (Wagner et al., 1996). Most preferably, the antisense oligonucleotides
25 comprise a complementary sequence of 20-30 bases. Although oligonucleotides may be chosen that are antisense to any region of the gene or mRNA transcripts, in preferred embodiments the antisense oligonucleotides correspond to N-terminal or 5' upstream sites such as translation initiation, transcription initiation or promoter sites. In addition, 3'-untranslated regions may be targeted. Targeting to mRNA splicing sites has also been used
30 in the art but may be less preferred if alternative mRNA splicing occurs. In addition, the antisense is targeted, preferably, to sites in which mRNA secondary structure is not expected (see, e.g., Sainio et al., 1994) and at which proteins are not expected to bind. Finally, although the listed sequences are cDNA sequences, one of ordinary skill in the art may easily

derive the genomic DNA corresponding to the cDNA of a breast cancer expressed polypeptide. Thus, the present invention also provides for antisense oligonucleotides which are complementary to the genomic DNA corresponding to breast cancer expressed nucleic acids. Similarly, the use of antisense to allelic or homologous cDNAs and genomic DNAs are enabled without undue experimentation.

In one set of embodiments, the antisense oligonucleotides of the invention may be composed of "natural" deoxyribonucleotides, ribonucleotides, or any combination thereof. That is, the 5' end of one native nucleotide and the 3' end of another native nucleotide may be covalently linked, as in natural systems, via a phosphodiester internucleoside linkage. These oligonucleotides may be prepared by art-recognized methods, which may be carried out manually or by an automated synthesizer. They also may be produced recombinantly by vectors.

In preferred embodiments, however, the antisense oligonucleotides of the invention also may include "modified" oligonucleotides. That is, the oligonucleotides may be modified in a number of ways which do not prevent them from hybridizing to their target but which enhance their stability or targeting or which otherwise enhance their therapeutic effectiveness. The term "modified oligonucleotide" as used herein describes an oligonucleotide in which (1) at least two of its nucleotides are covalently linked via a synthetic internucleoside linkage (i.e., a linkage other than a phosphodiester linkage between the 5' end of one nucleotide and the 3' end of another nucleotide) and/or (2) a chemical group not normally associated with nucleic acids has been covalently attached to the oligonucleotide. Preferred synthetic internucleoside linkages are phosphorothioates, alkylphosphonates, phosphorodithioates, phosphate esters, alkylphosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamides, carboxymethyl esters, and peptides.

The term "modified oligonucleotide" also encompasses oligonucleotides with a covalently modified base and/or sugar. For example, modified oligonucleotides include oligonucleotides having backbone sugars that are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified oligonucleotides may include a 2'-O-alkylated ribose group. In addition, modified oligonucleotides may include sugars such as arabinose instead of ribose. The present invention, thus, contemplates pharmaceutical preparations containing modified antisense molecules that are complementary to and

hybridizable with, under physiological conditions, breast cancer expressed nucleic acids, together with pharmaceutically acceptable carriers.

Antisense oligonucleotides may be administered as part of a pharmaceutical composition. Such a pharmaceutical composition may include the antisense oligonucleotides in combination with any standard physiologically and/or pharmaceutically acceptable carriers which are known in the art. The compositions should be sterile and contain a therapeutically effective amount of the antisense oligonucleotides in a unit of weight or volume suitable for administration to a patient. The term “pharmaceutically acceptable” means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients. The term “physiologically acceptable” refers to a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism. The characteristics of the carrier will depend on the route of administration. Physiologically and pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials, which are well known in the art.

Expression of breast cancer nucleic acid molecules can also be determined using protein measurement methods to determine expression of SEQ ID NOs:1-51, e.g., by determining the expression of polypeptides encoded by SEQ ID NOs:1-51 (SEQ ID NOs: 52-102, respectively). Preferred methods of specifically and quantitatively measuring proteins include, but are not limited to: mass spectroscopy-based methods such as surface enhanced laser desorption ionization (SELDI; e.g., Ciphergen ProteinChip System), non-mass spectroscopy-based methods, antibody-capture protein arrays and immunohistochemistry-based methods such as 2-dimensional gel electrophoresis.

SELDI methodology may be used, through procedures known to those of ordinary skill in the art, to vaporize microscopic amounts of tumor protein and to create a “fingerprint” of individual proteins, thereby allowing simultaneous measurement of the abundance of many proteins in a single sample. Preferably SELDI-based assays may be utilized to classify breast cancer tumors. Such assays preferably include, but are not limited to the following examples. Gene products discovered by RNA microarrays may be selectively measured by specific (antibody mediated) capture to the SELDI protein disc (e.g., selective SELDI). Gene products discovered by protein screening (e.g., with 2-D gels), may be resolved by “total protein SELDI” optimized to visualize those particular markers of interest from among SEQ ID NOs:1-51. Predictive models of tumor classification from SELDI measurement of multiple markers from among SEQ ID NOs:1-51 may be utilized for the SELDI strategies. In an

additional embodiment a set of primary lymph node-negative premenopausal breast cancer tissues may be preferably utilized to determine the risk classification of breast cancer based on SELDI results.

The invention also involves agents such as polypeptides that bind to breast cancer-associated polypeptides, i.e., SEQ ID NOs:52-102. Such binding agents can be used, for example, in screening assays to detect the presence or absence of breast cancer-associated polypeptides and complexes of breast cancer-associated polypeptides and their binding partners and in purification protocols to isolate breast cancer-associated polypeptides and complexes of breast cancer-associated polypeptides and their binding partners. Such agents also may be used to inhibit the native activity of the breast cancer-associated polypeptides, for example, by binding to such polypeptides.

The invention, therefore, embraces peptide binding agents which, for example, can be antibodies or fragments of antibodies having the ability to selectively bind to breast cancer-associated polypeptides. Antibodies include polyclonal and monoclonal antibodies, prepared according to conventional methodology.

Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W.R. (1986) The Experimental Foundations of Modern Immunology Wiley & Sons, Inc., New York; Roitt, I. (1991) Essential Immunology, 7th Ed., Blackwell Scientific Publications, Oxford). The pFc' and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the pFc' region has been enzymatically cleaved, or which has been produced without the pFc' region, designated an F(ab')₂ fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Proceeding further, Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.

Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the

paratope (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of conspecific or heterospecific antibodies while retaining the epitopic specificity of the original antibody. This is most clearly manifested in the development and use of "humanized" antibodies in which non-human CDRs are covalently joined to human FR and/or Fc/pFc' regions to produce a functional antibody. See, e.g., U.S. patents 4,816,567, 5,225,539, 5,585,089, 5,693,762 and 5,859,205.

Fully human monoclonal antibodies also can be prepared by immunizing mice transgenic for large portions of human immunoglobulin heavy and light chain loci. Following immunization of these mice (e.g., XenoMouse (Abgenix), HuMAb mice (Medarex/GenPharm)), monoclonal antibodies can be prepared according to standard hybridoma technology. These monoclonal antibodies will have human immunoglobulin amino acid sequences and therefore will not provoke human anti-mouse antibody (HAMA) responses when administered to humans.

Thus, as will be apparent to one of ordinary skill in the art, the present invention also provides for F(ab')₂, Fab, Fv and Fd fragments; chimeric antibodies in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric F(ab')₂ fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric Fab fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; and chimeric Fd fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced by homologous human or non-human sequences. The present invention also includes so-called single chain antibodies.

Thus, the invention involves polypeptides of numerous size and type that bind specifically to polypeptides selected from SEQ ID NOs:52-102, and complexes of both breast cancer-associated polypeptides and their binding partners. These polypeptides may be derived also from sources other than antibody technology. For example, such polypeptide binding agents can be provided by degenerate peptide libraries which can be readily prepared

in solution, in immobilized form or as phage display libraries. Combinatorial libraries also can be synthesized of peptides containing one or more amino acids. Libraries further can be synthesized of peptoids and non-peptide synthetic moieties.

Phage display can be particularly effective in identifying binding peptides useful according to the invention. Briefly, one prepares a phage library (using e.g. m13, fd, or lambda phage), displaying inserts from 4 to about 80 amino acid residues using conventional procedures. The inserts may represent, for example, a completely degenerate or biased array. One then can select phage-bearing inserts which bind to the breast cancer-associated polypeptide. This process can be repeated through several cycles of reselection of phage that bind to the breast cancer-associated polypeptide. Repeated rounds lead to enrichment of phage bearing particular sequences. DNA sequence analysis can be conducted to identify the sequences of the expressed polypeptides. The minimal linear portion of the sequence that binds to the breast cancer-associated polypeptide can be determined. One can repeat the procedure using a biased library containing inserts containing part or all of the minimal linear portion plus one or more additional degenerate residues upstream or downstream thereof. Yeast two-hybrid screening methods also may be used to identify polypeptides that bind to the breast cancer-associated polypeptides.

Thus, the breast cancer-associated polypeptides of the invention, including fragments thereof, can be used to screen peptide libraries, including phage display libraries, to identify and select peptide binding partners of the breast cancer-associated polypeptides of the invention. Such molecules can be used, as described, for screening assays, for purification protocols, for interfering directly with the functioning of breast cancer-associated polypeptides and for other purposes that will be apparent to those of ordinary skill in the art. For example, isolated breast cancer-associated polypeptides can be attached to a substrate (e.g., chromatographic media, such as polystyrene beads, a filter, or an array substrate), and then a solution suspected of containing the binding partner may be applied to the substrate. If a binding partner that can interact with breast cancer-associated polypeptides is present in the solution, then it will bind to the substrate-bound breast cancer-associated polypeptide. The binding partner then may be isolated.

As detailed herein, the foregoing antibodies and other binding molecules may be used for example, to identify tissues expressing protein or to purify protein. Antibodies also may be coupled to specific diagnostic labeling agents for imaging of cells and tissues that express breast cancer-associated polypeptides or to therapeutically useful agents according to

standard coupling procedures. Diagnostic agents include, but are not limited to, barium sulfate, iocetamic acid, iopanoic acid, ipodate calcium, diatrizoate sodium, diatrizoate meglumine, metrizamide, tyropanoate sodium and radiodiagnostics including positron emitters such as fluorine-18 and carbon-11, gamma emitters such as iodine-123,
5 technitium-99m, iodine-131 and indium-111, nuclides for nuclear magnetic resonance such as fluorine and gadolinium.

The invention further includes protein microarrays for analyzing expression of breast cancer-associated peptides selected from SEQ ID NOs:52-102. In this aspect of the invention, standard techniques of microarray technology are utilized to assess expression of
10 the breast cancer-associated polypeptides and/or identify biological constituents that bind such polypeptides. The constituents of biological samples include antibodies, lymphocytes (particularly T lymphocytes), and the like. Protein microarray technology, which is also known by other names including: protein chip technology and solid-phase protein array technology, is well known to those of ordinary skill in the art and is based on, but not limited
15 to, obtaining an array of identified peptides or proteins on a fixed substrate, binding target molecules or biological constituents to the peptides, and evaluating such binding. See, e.g., G. MacBeath and S.L. Schreiber, "Printing Proteins as Microarrays for High-Throughput Function Determination," *Science* 289(5485):1760-1763, 2000.

Preferably antibodies or antigen binding fragments thereof that specifically bind
20 polypeptides selected from the group consisting of SEQ ID NOs:52-102 are attached to the microarray substrate in accordance with standard attachment methods known in the art. These arrays can be used to quantify the expression of the polypeptides identified herein.

In some embodiments of the invention, one or more control peptide or protein molecules are attached to the substrate. Preferably, control peptide or protein molecules
25 allow determination of factors such as peptide or protein quality and binding characteristics, reagent quality and effectiveness, hybridization success, and analysis thresholds and success.

The use of such methods to determine expression of breast cancer nucleic acids from among SEQ ID NOs:1-51 and/or proteins from among SEQ ID Nos:52-102 can be done with routine methods known to those of ordinary skill in the art and the expression determined by
30 protein measurement methods may be correlated to MAI levels and used as a prognostic method for selecting treatment strategies for breast cancer patients.

Examples

Introduction

To establish a prognostic tool for designing breast cancer treatment regimens, expression patterns in primary breast cancer specimens were assessed and correlated with clinical outcome. Primary breast cancer tumors from premenopausal women with no lymph node metastases at the time of initial presentation were classified using the Mitotic Activity Index (MAI), which has been shown to predict disease-free survival in this type of disease. RNA was isolated, hybridized with Affymetrix HuFL human expression arrays, and analyzed to ascertain which genes discriminate the two groups.

Methods

Breast Cancers Used for RNA Microarray Expression Analysis

Primary frozen breast cancers from premenopausal women with no lymph node metastases at the time of initial presentation were assembled from material discarded following routine surgical removal for diagnostic purposes. Institutional review and human subjects approval for this project was obtained from Brigham and Women's Hospital. Fresh tissue was frozen in liquid nitrogen, and a single fragment split for confirmatory histology and RNA isolation. Individual fragments of frozen tumor tissues (estimated as 500 mg minimum) were split by fracturing under liquid nitrogen, and a portion processed for confirmatory histology using standard methods. The remaining tissue was used for synchronous RNA, protein, and DNA isolations with TRIzol reagents (Life Technologies, Inc., Rockville, MD) using standard methods. Only tumors where the actual frozen tissue contained >50% tumor cells were used.

Mitotic Activity Index

All tumors were classified by Mitotic Activity Index (Baak et al., 1989; van Diest et al., 1991; van Diest et al., 1992(a); Uytterlinde et al., 1990; van Diest et al., 1992(b); Jannink et al., 1996; Baak et al., 1992; Baak et al., 1993) using paraffin H&E stained tissues sections prepared for diagnostic purposes at the time of excision. The MAI is the total number of mitoses counted in 10 consecutive high-power fields (objective, x40; numeric aperture, 0.75; field diameter, 450 microns) in the most cellular area at the periphery of the tumor, with the subjectively highest mitotic activity (Jannink et al., 1995). Risk groups have previously been

defined using a threshold of 10 mitoses/unit area (Tosi et al., 1986; Jannink et al., 1995; Theissig et al., 1996). Tumors with $MAI \geq 10$ were assigned to the high risk group, and those with $MAI \leq 3$ to the low risk group.

5 *Microarray Expression Analysis*

RNA from 27 qualifying tumors was reverse transcribed and resultant cDNA used for *in vitro* transcriptional synthesis of fluorescently labeled nucleic acid probes which were then hybridized to Affymetrix HuFL human expression arrays (approximately 7100, probe sets, estimated 5800 unique genes). Hybridization images were analyzed with Affymetrix
10 software to generate a data matrix of named probes by quantitative expression level in each tissue. RNA labeling, microarray hybridization, and microarray analysis were performed as per vendor's instructions for HuGeneFL array (Affymetrix, Santa Clara, CA). Four tumors were excluded from analysis because they failed to meet quality control criteria for microarray hybridization: 3 cases had low hybridization signal, one case had high
15 background.

Results

Analysis of 23 primary breast cancer specimens from premenopausal lymph node negative women were split between two prognostic groups (Low MAI, $MAI \leq 3$, $n=11$ and
20 High MAI, $MAI \geq 10$, $n=12$) and was accomplished as follows. Affymetrix HuFL expression values were normalized by scaling so the sum of AD (AD units are the quantitative expression units used by Affymetrix) values in each sample was 3,000,000; genes for which RNA abundance was absent or marginal were reset to a value of 0, then any values less than 20 were reset to 20. The result is the GPT dataset, which was then log transformed and
25 discriminating genes selected by t-test comparison of the logged data between low and high MAI groups. Significance cutoffs for the t-tests used Permax < 0.96 based on 10,000 random permutations of the data. Permax is a data analysis software tool for testing the significance of gene expression. It has been presented by Mutter, et al., 8th International Workshop on Chromosomes in Solid Tumors, Tucson, AZ, 2000; and is available online at
30 biowww.dfci.harvard.edu/~gray/permax.html and from Robert J. Gray, Department of Biostatistical Science, Dana-Farber Cancer Institute, 44 Binney Street Boston, MA 02115. Permax details enclosed therein are incorporated by reference herein. Seventy eight of 7070 Affymetrix probe sets were selected by Permax.

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Filters for minimum divergence between the average expression values of the two groups (Low vs. High MAI) were applied as follows: ratio of means ≥ 2 , and difference between means ≥ 100 . It was determined that 51/78 genes passed these filters. The final 51 selected genes which discriminate between low and high MAI subgroups appear in Table 1 and as SEQ ID NOs:1-51. Average expression in high MAI tumors and low MAI tumors is shown as HX and LX, respectively.

Table 1. Gene list identifying 51 genes that discriminate low from high MAI breast cancers.

SEQ ID NO	Short Name	GenBank Acc.No.	Permax	HX	LX	FOLDABS	DIFFABS
1	ABCB2	X57522	0.9577	501	83	6.0	417
2	ACTA2	X13839	0.7131	3098	6152	2.0	3054
3	AMD1	M21154	0.0808	257	50	5.1	207
4	APM2	D45370	0.3317	590	2682	4.5	2092
5	ASAH	U70063	0.8435	360	990	2.8	630
6	BARD1	U76638	0.5637	242	102	2.4	140
7	CCNH	U11791	0.9104	104	204	2.0	100
8	CCT2	U91327	0.8801	280	109	2.6	171
9	CDC20	U05340	0.0669	579	20	29.0	559
10	CDC34	L22005	0.6979	182	41	4.4	141
11	CDKN3	U02681	0.0072	454	63	7.2	391
12	CKS1	X54941	0.8823	539	219	2.5	320
13	CKS2	X54942	0.1881	413	119	3.5	294
14	COX7A1	M83186	0.9223	89	326	3.6	236
15	CPA3	M73720	0.8234	132	357	2.7	225
16	CPE	X51405	0.1984	80	243	3.0	163
17	CX3CR1	U20350	0.0317	70	328	4.7	258
18	DLG4	U83192	0.3427	20	179	8.9	159
19	DOC1	U53445	0.927	122	276	2.3	154
20	DXS9879E	X92896	0.9448	744	331	2.3	413
21	E2-EPF	M91670	0.9602	324	20	16.2	304
22	ElastinAlt2	U77846	0.8368	417	2210	5.3	1792
23	GTF2A1	U14193	0.7495	528	249	2.1	279
24	GUA5MPST	U10860	0.6129	599	114	5.2	485
25	H2AFX	X14850	0.8106	496	193	2.6	303
26	H2BFA	M60750	0.2334	508	143	3.6	365
27	Hevin	X86693	0.7484	529	1686	3.2	1157
28	HNRPH2	U01923	0.9056	106	231	2.2	126
29	HPV16E1Bind	U96131	0.2439	194	78	2.5	116
30	IDUA	M74715	0.1712	176	594	3.4	418
31	IGF1	X57025	0.9213	79	265	3.4	186
32	IQGAP2	U51903	0.9517	137	321	2.3	184
33	ISG15	M13755	0.9316	2133	386	5.5	1747
34	JAG1	U61276	0.9466	79	264	3.3	185
35	LAMA2	Z26653	0.8882	31	213	6.8	182
36	LAMB2	X79683	0.083	156	658	4.2	502
37	LBR	L25931	0.5991	221	68	3.2	153
38	MMP2	M55593	0.93	1765	3670	2.1	1905
39	MMSDH	M93405	0.9072	297	669	2.3	372
40	MYH11	AF001548	0.3109	164	777	4.7	612
41	MYLK	U48959	0.8351	158	680	4.3	522
42	PDE4A	L20965	0.8912	34	176	5.2	142
43	SCNN1A	X76180	0.694	352	864	2.5	511
44	SCYB10	X02530	0.4416	528	83	6.4	445
45	SNRPB	X17567	0.8965	1473	638	2.3	835
46	STAT1	M97936	0.9553	440	20	22.0	420
47	TAF2A	X07024	0.6819	193	65	2.9	127
48	TCEAL1	M99701	0.5595	241	749	3.1	508
49	TPM1	Z24727	0.5676	1266	2533	2.0	1267
50	TPS2	M33493	0.3638	194	892	4.6	698
51	UBCH10	U73379	0.1972	1519	639	2.4	880

Several features of selected genes provide reassurance that low frequency random events were not the cause of expression differences between groups. A review of the 51 selected genes (Table 1) shows that five pairs of genes known to be co-expressed were
5 selected independently (two carboxypeptidases, two histones, two cdc28, two ubiquitins, two laminins, and myosin/tropomyosin), and reciprocal regulation of ligand and receptor, a common regulatory pattern, occurred once (laminin and lamin receptor) amongst genes selected.

The first expectation is that genes whose expression is linked to cell division would be
10 represented in this comparison of tumors whose mitotic activity differs systematically. This was in fact the largest category of selected genes, with expression of 11/12 cell cycle genes greatest in the high MAI group. Genes which are preferentially expressed (at higher levels) in the low MAI group include those encoding extracellular matrix or enzymes which may remodel extracellular matrix (proteolytic enzymes).

The gene expression data presented in Table 1 can be used to generate an expression
15 matrix of 51 selected genes by 23 tissues examined. Using standard clustering algorithms, dendrograms can be provided on the borders of the matrix (e.g., using Wards linkage and Euclidean distance) to show cluster relationships between tissues and genes. Similarly, a gene expression matrix can be generated using data normalized by standard deviation for
20 each gene [STD(GPT)]. Dendrograms on borders of the matrix can be provided to show cluster relationships between tissues and genes. In this type of matrix, clustering of genes is based upon relative changes without bias due to absolute expression level, because each gene is expressed in standard deviation from the mean for that specific gene. However, unlike the other expression matrix described above, the absolute magnitude of expression cannot be
25 directly inferred from this plot.

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5 The present invention is not limited in scope by the examples provided, since the examples are intended as illustrations of various aspects of the invention and other functionally equivalent embodiments are within the scope of the invention. Various modifications of the invention in addition to those shown are described herein will become apparent to those skilled in the art for the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily
10 encompassed by each embodiment of the invention. All references, patents, and patent publications that are recited in this application are incorporated in their entirety herein by reference.

We claim:

Claims

1. A method for diagnosing breast cancer in a subject suspected of having breast cancer comprising:

5 obtaining from the subject a breast tissue sample suspected of being cancerous,
determining the expression of a set of nucleic acid molecules or expression products thereof in the breast tissue sample, wherein the set of nucleic acid molecules comprises at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

10 2. The method of claim 1, wherein the set of nucleic acid molecules comprises at least 3 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

3. The method of claim 1, wherein the set includes at least 4 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

15 4. The method of claim 1, wherein the set includes at least 5 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

5. The method of claim 1, wherein the set includes at least 10 nucleic acid molecules
20 selected from the group consisting of SEQ ID NOs:1-51.

6. The method of claim 1, wherein the set includes at least 15 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

25 7. The method of claim 1, wherein the set includes at least 20 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

8. The method of claim 1, wherein the set includes at least 30 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

30 9. The method of claim 1, wherein the set includes at least 40 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

10. The method of claim 1, further comprising:

determining the expression of the set of nucleic acid molecules or expression products thereof in a non-cancerous breast tissue sample, and comparing the expression of the set of nucleic acid molecules or expression products thereof in the breast tissue sample suspected of
5 being cancerous and the non-cancerous breast tissue sample.

11. A method for identifying a set of nucleic acid markers or expression products thereof effective for determining the prognosis of cancer, comprising:

obtaining a plurality of tumor tissue samples from a plurality of subjects afflicted with
10 cancer,

classifying the plurality of tumor tissue samples according to mitotic activity index (MAI) into high MAI and low MAI groups,

determining differences in the expression of a plurality of nucleic acid molecules or expression products thereof in the tumor tissue samples, and

15 selecting as a set of nucleic acid markers the nucleic acid molecules or expression products thereof which are differentially expressed in the high MAI and the low MAI groups,

wherein the set of nucleic acid markers or expression products thereof effective for determining poor prognosis of cancer comprises one or more nucleic acid molecules or expression products thereof which are preferentially expressed in high MAI tumor tissue
20 samples, and wherein the set of nucleic acid markers or expression products thereof effective for determining good prognosis of cancer comprises one or more nucleic acid molecules or expression products thereof which are preferentially expressed in low MAI tumor tissue samples.

25 12. The method of claim 11, wherein the cancer is breast cancer.

13. The method of claim 11, wherein the differences in the expression of a plurality of nucleic acid molecules are determined by a method selected from the group consisting of nucleic acid hybridization and nucleic acid amplification.

30 14. The method of claim 13, wherein the nucleic acid hybridization is performed using a solid-phase nucleic acid molecule array.

15. A method for selecting a course of treatment of a subject having or suspected of having cancer, comprising:

obtaining from the subject a tissue sample suspected of being cancerous,

determining the expression of a set of nucleic acid markers or expression products

5 thereof which are differentially expressed in high MAI tumor tissue samples to determine the MAI of the tissue sample of the subject, and

selecting a course of treatment appropriate to the cancer of the subject.

16. The method of claim 15 wherein the cancer is breast cancer.

10

17. The method of claim 16, further comprising:

determining the expression of a set of nucleic acid markers that are differentially expressed in low MAI breast tumor tissue samples.

15 18. The method of claim 15, wherein the expression of a set of nucleic acid markers is determined by a method selected from the group consisting of nucleic acid hybridization and nucleic acid amplification.

19. The method of claim 18, wherein the nucleic acid hybridization is performed using a
20 solid-phase nucleic acid molecule array.

20. A method for evaluating treatment of cancer, comprising:

obtaining a first determination of the expression of a set of nucleic acid molecules or expression products thereof, which are differentially expressed in high MAI tumor tissue
25 samples to determine the MAI of the tissue sample from a subject undergoing treatment for cancer,

obtaining a second determination of the expression of a set of nucleic acid molecules or expression products thereof, which are differentially expressed in high MAI tumor tissue samples to determine the MAI of the second tissue sample from the subject after obtaining
30 the first determination,

comparing the first determination of expression to the second determination of expression as an indication of evaluation of the treatment.

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21. The method of claim 20, wherein the cancer is breast cancer.

22. The method of claim 21, further comprising:

determining the expression of a set of nucleic acid markers which are differentially
5 expressed in low MAI breast tumor tissue samples.

23. The method of claim 20, wherein the expression of a set of nucleic acid markers is
determined by a method selected from the group consisting of nucleic acid hybridization and
nucleic acid amplification.

10 24. The method of claim 20, wherein the nucleic acid hybridization is performed using a
solid-phase nucleic acid molecule array.

25. A solid-phase nucleic acid molecule array consisting essentially of at least two nucleic
15 acid molecules selected from the group consisting of SEQ ID NOs:1-51 fixed to a solid
substrate.

26. The solid-phase nucleic acid molecule array of claim 24, further comprising at least
one control nucleic acid molecule.

20 27. The solid-phase nucleic acid molecule array of claim 24, wherein the set of nucleic
acid molecules comprises at least 3 nucleic acid molecules selected from the group consisting
of SEQ ID NOs:1-51.

25 28. The solid-phase nucleic acid molecule array of claim 24, wherein the set includes at
least 4 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

29. The solid-phase nucleic acid molecule array of claim 24, wherein the set includes at
least 5 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

30 30. The solid-phase nucleic acid molecule array of claim 24, wherein the set includes at
least 10 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

31. The solid-phase nucleic acid molecule array of claim 24, wherein the set includes at least 15 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

32. The solid-phase nucleic acid molecule array of claim 24, wherein the set includes at least 20 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

33. The solid-phase nucleic acid molecule array of claim 24, wherein the set includes at least 30 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

34. The solid-phase nucleic acid molecule array of claim 24, wherein the set includes at least 40 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51.

35. The solid-phase nucleic acid molecule array of claim 24, wherein the solid substrate comprises a material selected from the group consisting of glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, and nylon.

36. The solid-phase nucleic acid molecule array of claim 24, wherein the nucleic acid molecules are fixed to the solid substrate by covalent bonding.

37. A solid-phase protein microarray comprising at least two antibodies or antigen-binding fragments thereof, that specifically bind at least two different polypeptides selected from the group consisting of SEQ ID NOs:52-102, fixed to a solid substrate.

38. The protein microarray of claim 37, wherein the microarray further comprises an antibody or antigen-binding fragment thereof, that binds specifically to a cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs:52-102.

39. The protein microarray of claim 38, wherein the cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs:52-102 is a breast cancer associated polypeptide.

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40. The protein microarray of claim 37, further comprising at least one control polypeptide molecule.

41. The protein microarray of claim 37, wherein the antibodies are monoclonal or polyclonal antibodies.

42. The protein microarray of claim 37, wherein the antibodies are chimeric, human, or humanized antibodies.

43. The protein microarray of claim 37, wherein the antibodies are single chain antibodies.

44. The protein microarray of claim 37, wherein the antigen-binding fragments are F(ab')₂, Fab, Fd, or Fv fragments.

45. A method for identifying lead compounds for a pharmacological agent useful in the treatment of breast cancer, comprising:

contacting a breast cancer cell or tissue with a candidate pharmacological agent,

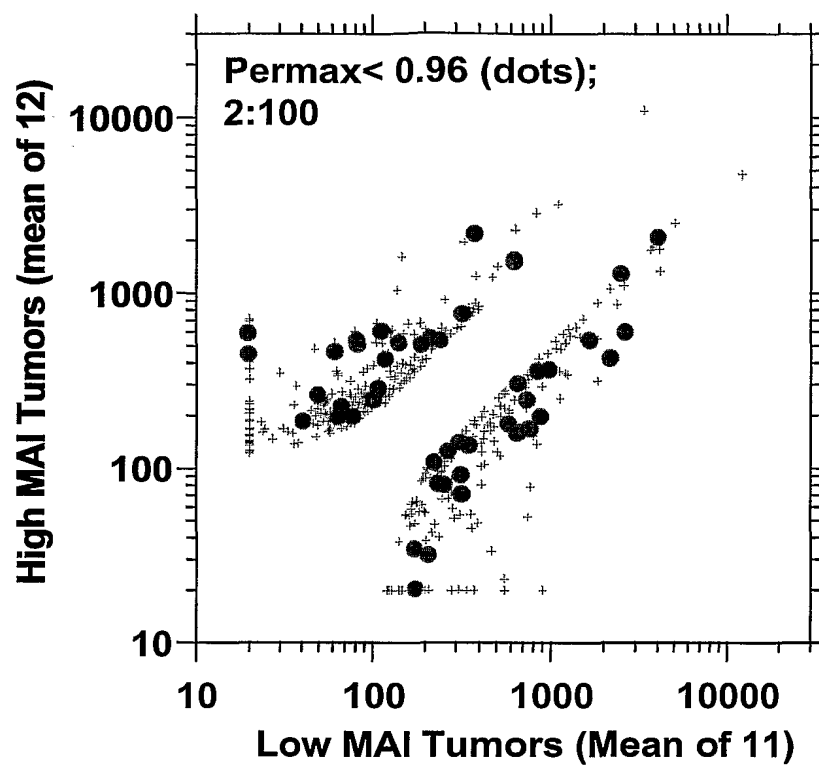
determining the expression of a set of nucleic acid molecules in the breast cancer cell

or tissue sample under conditions which, in the absence of the candidate pharmacological agent, permit a first amount of expression of the set of nucleic acid molecules wherein the set of nucleic acid molecules comprises at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-51, and

detecting a test amount of the expression of the set of nucleic acid molecules, wherein a decrease in the test amount of expression in the presence of the candidate pharmacological agent relative to the first amount of expression indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which is useful in the treatment of breast cancer.

46. The method of claim 45, wherein the set of nucleic acid molecules is differentially expressed in high MAI breast tumor tissue samples.

1/1

**Fig. 1**

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Baak, Jan

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<213> Homo Sapiens

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<212> DNA

<213> Homo Sapiens

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- 12 -

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 <213> Homo Sapiens

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- 13 -

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<212> DNA
<213> Homo Sapiens

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- 14 -

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 <213> Homo Sapiens

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<212> DNA

<213> Homo Sapiens

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<210> 19
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<212> DNA
<213> Homo Sapiens

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<210> 20
 <211> 599
 <212> DNA
 <213> Homo Sapiens

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 gcgccaggtc cgggcagaga cgccgcgtct gccgcagggg gtcacgaatg cggccgcaca 180
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<210> 21
 <211> 890
 <212> DNA
 <213> Homo Sapiens

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<210> 22
 <211> 1449
 <212> DNA
 <213> Homo Sapiens

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 <222> (1316)..(1316)
 <223> n = a, c, g, or t

<220>
 <221> Unsure
 <222> (1360)..(1360)
 <223> n = a, c, g, or t

<220>
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 <223> n = a, c, g, or t

<220>
 <221> Unsure
 <222> (1369)..(1369)
 <223> n = a, c, g, or t

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ccttggtatg atttaatctg ccttcaactg ttggcctggn tggggnnang ggctctgctt     1380
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cctggcttc                                     1449

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<210> 23
<211> 736
<212> DNA
<213> Homo Sapiens

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gtagaaagaa acttgtaact ctgtagcctc ttacatcacc tttattatac agcatgaaaa     660
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<210> 24

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<211> 2212

<212> DNA

<213> Homo Sapiens

<400> 24

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cgatggctct	gtgcaacgga	gactccaagc	tggagaatgc	tggaggagac	cttaaggatg	180
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<210> 25

<211> 1585

<212> DNA

<213> Homo Sapiens

<400> 25

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<210> 26
<211> 847
<212> DNA
<213> Homo Sapiens

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<210> 27
<211> 2808

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<212> DNA

<213> Homo Sapiens

<400> 27

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ttgacagagc agcagaatat caactccagt agacttgaat gtgcctctgg gcaaagaagc	180
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<212> DNA

<213> *Homo Sapiens*

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 <211> 2203
 <212> DNA
 <213> Homo Sapiens

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<211> 2155
<212> DNA
<213> Homo Sapiens

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<212> DNA
<213> Homo Sapiens

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<212> DNA
<213> Homo Sapiens

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<211> 1172
<212> DNA
<213> Homo Sapiens

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<212> DNA
<213> Homo Sapiens

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 <213> Homo Sapiens

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<211> 5257

<212> DNA

<213> Homo Sapiens

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tctgctagag	gtgactgggg	tggcagatcc	cacgggggtg	ggtgaaggat	tctcctatgt	3060
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gacagtgaca	ggaacagatg	cagaccttcg	tcgcctttcc	ctgaaaaatg	ccaagcaact	3180
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tcgaaaattt	gccctttttg	atgaacaaca	tcgggaagag	atgcgaaaag	aacggcggag	3840
gattcaagag	caactgaggc	ggcttaagag	gaaccaggaa	aaggagaagc	ttaaggggtcc	3900
tcctgagaag	aagcccaaga	aatgaagga	gcgtcctgac	ctaaaactga	aatgtggggc	3960

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atgtggtgcc attggacaca tgaggactaa caaattctgc cccctctatt atcaaacaaa 4020
tgcgccacct tccaaccctg ttgccatgac agaagaacag gaggaggagt tggaaaagac 4080
agtcattcat aatgataatg aagaacttat caaggttgaa gggaccaaaa ttgtcttggg 4140
gaaacagcta attgagagtg cggatgaggt tcgcagaaaa tctctggttc tcaagtttcc 4200
taaacagcag cttcctccaa agaagaaacg gcgagttgga accactgttc actgtgacta 4260
tttgaataga cctcataagt ccatccaccg gcgcgcaca gaccctatgg tgacgctgtc 4320
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<210> 48
<211> 1174
<212> DNA
<213> Homo Sapiens

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gtcacacggg ggcacctcga ggagaggacg actaggagca cacggcccgg aaaggtccag 120
gtcaggggaag ggaataactg tgcttgaaga agaaaattcc caacatggac aaaccacgca 180
aagaaaatga agaagagccg cagagccgcc caagaccgat gaggagaggc ctccggtgga 240
gcactctccc gaaaagcagt ccccgagga gcagtcttcg gaggagcagt cctcggagga 300

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ggagttcttt cctgaggagc tcttgctga gctcctgct gagatgctcc tctcggagga 360
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ctccttgttg agtaggaaaa cataaccttg aagaaggaat ctttaaagaa aggttggctc 480
gttctcgccc gcaatttaga ggggacatac atggcagaaa tttaaagcaat gaggagatga 540
tacaggcagc agatgagcta gaagagatga aaagagtaag aaacaaactg atgataatgc 600
actggagggc aaaacggggc ggtccttacc ctatttaatg tgttcggcct ttaattctgt 660
tttgctgct atagtattgc cattgccacc tggactttct gtttgcattt tcttaatgcc 720
ttttccctat ttctgaattt taactttttg tgaggcttta ttttagatgt ttagcatgta 780
actcgcttaa agttgaggtt tccccctaaa atctacaagt ttccctcttt cagtcatgag 840
ccctacacat ttgcatgaaa gatgtacata tatattgtga acgaaaaaag caattttcaa 900
atggtatata tgtatcccat tttgtaaaaa atgtatatta tatattaata tgcaaagaaa 960
aagctaaaag tatagacttc aaaggcataa cagtggttgt gtggttaagat ataggtgatt 1020
ttttaaat tttgtttatc tgaatttctc attttttcag gacaaacgtt ttacttgtgt 1080
tgcaaaaata tataatgaaa aaatcacaca attttgaaga aaactgtcaa tcagcttata 1140
acgacaatgt ggcacttaat aaatacttgt cagg 1174

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<210> 49
<211> 1569
<212> DNA
<213> Homo Sapiens

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<400> 49
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gggacgatga tatgaggtaa gcacacaaga gctatggaca agacaaggtc taaaggattt 180
tgaatacaaa gcagaaatat ttcgaccttc tcatttcttg ggtgggagtg gggagtgttc 240
attaagtaca tatgacaaga gggagtgtgg ggagaagggtg aaacagtaga ctacatttat 300
ggattaagta gggaatgtga acaaagatgt taaagtcag gcgatccggt agacagatta 360
cacagaaggg gaccgaagat gaactggaca aatactctga ggctctcaaa gatgcccagg 420
agaagctgga gctggcagag aaaaaggcca ccgatgctga agccgacgta gcttctctga 480
acagacgcat ccagctgggt gaggaagagt tggatcgtgc ccaggagcgt ctggcaacag 540
ctttgcagaa gctggaggaa gctgagaagg cagcagatga gagtgagaga ggcataaag 600
tcattgagag tcgagcccaa aaagatgaag aaaaaatgga aattcaggag atccaactga 660

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aagaggccaa	gcacattgct	gaagatgccg	accgcaaata	tgaagaggtg	gcccgtaagc	720
tggtcatcat	tgagagcgac	ctggaacgtg	cagaggagcg	ggctgagctc	tcagaaggcc	780
aagtccgaca	gctggaagaa	caattaagaa	taatggatca	gaccttgaaa	gcattaatgg	840
ctgcagagga	taagtactcg	cagaaggaag	acagatatga	ggaagagatc	aaggtccttt	900
ccgacaagct	gaaggaggct	gagactcggg	ctgagtttgc	ggagagggtca	gtaactaaat	960
tggagaaaag	cattgatgac	ttagaagaga	aagtgctcat	gccaaagaag	aaaaccttag	1020
tatgcatcag	atgctggatc	agactttact	ggagttaaac	aacatgtgaa	aacctcctta	1080
gctgcgacca	cattctttca	ttttgttttg	ttttgttttg	tttttaaaca	cctgcttacc	1140
ccttaaatgc	aatttattta	cttttaccac	tgtcacagaa	acatccacaa	gataccagct	1200
aggtcagggg	gtggggaaaa	cacatacaaa	aagcaagccc	atgtcagggc	gatcctgggt	1260
caaatgtgcc	atctcccg	ttgatgctgc	cacactttgt	agagagttta	gcaacacagt	1320
gtgcttagtc	agtgtaggaa	tcctcactaa	agcagaagaa	gttcatttcc	tttctgattg	1380
gcacacgtgc	agctcatgac	aatctgtagg	ataacaatca	gtgtggattt	ccactctttt	1440
cagtccttca	tgttaaagat	ttagacacca	catacaactg	gtaaaggacg	ttttcttgag	1500
agttttaact	atatgtaaac	attgtataat	gatatggaat	aaaatgcaca	ttttaggaca	1560
ttttctaaa						1569

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<210> 50
<211> 1081
<212> DNA
<213> Homo Sapiens.
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<400>	50						
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agtgggcatac	gttgggggtc	aggaggcccc	caggagcaag	tggccctggc	aggtgagcct		120
gagagtccgc	gaccgatact	ggatgcactt	ctgcgggggc	tccctcatcc	acccccagtg		180
ggtgctgacc	gcagcgcact	gcgtgggacc	ggacgtcaag	gatctggccg	ccctcagggt		240
gcaactgcgg	gagcagcacc	tctactacca	ggaccagctg	ctgccggtca	gcaggatcat		300
cgtgcaccca	cagttctaca	ccgcccagat	cggagcggac	atcgccctgc	tggagctgga		360
ggagccggtg	aaggtctcca	gccacgtcca	cacggtcacc	ctgccccctg	cctcagagac		420
cttccccccg	gggatgccgt	gctgggtcac	tggctggggc	gatgtggaca	atgatgagcg		480
cctcccaccg	ccatttcctc	tgaagcaggt	gaaggtcccc	ataatggaaa	accacatttg		540
tgacgcaaaa	taccaccttg	gcgcctacac	gggagacgac	gtccgcaticg	tccgtgacga		600
catgctgtgt	gccgggaaca	cccggaggga	ctcatgccag	ggcgactccg	qaqqqcccct		660

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gggtgtgcaag gtgaatggca cctgggtgca ggcgggctg gtcagctggg gcgagggctg 720
tgcccagccc aaccggcctg gcatctacac ccgtgtcacc tactacttgg actggatcca 780
ccactatgtc cccaaaaagc cgtgagtcag gcctgggggtg tccacctggg tccactggagg 840
accagccctt cctgtccaaa acaccactgc ttccctaccca ggcgggcgact gccccccaca 900
ccttccctgc ccgctcctga gtgccccttc ctgtcctaag ccccttgctc tcttctgagc 960
cccttccctt gtcttgagga cccttcccca tcttgagccc ccttccctgt cctaagcctg 1020
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c 1081

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<210> 51
<211> 783
<212> DNA
<213> Homo Sapiens

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<400> 51
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cccagccgcc actagcgtcg ccgccgcccg taaaggagct gagccgagcg ggggcgcccgc 120
ccgggggtccg gtgggcaaaaa ggctacagca ggagctgatg accctcatga tgtctggcga 180
taaagggatt tctgccttcc ctgaatcaga caaccttttc aaatgggtag ggaccatcca 240
tggagcagct ggaacagtat atgaagacct gaggtataag ctctcgctag agttccccag 300
tggtaccctt tacaatgcgc ccacagtga gttcctcag cctgctatc accccaacgt 360
ggacacccag ggtaacatat gcctggacat cctgaaggaa aagtgggtctg ccctgtatga 420
tgtcaggacc attctgctct ccattccagag ccttctagga gaacccaaca ttgatagtcc 480
cttgaacaca catgctgccg agctctggaa aaaccccaca gcttttaaga agtacctgca 540
agaaacctac tcaaagcagg tcaccagcca ggagccctga cccaggctgc ccagcctgtc 600
cttgtgtcgt ctttttaatt tttccttaga tggctctgtc tttttgtgat ttctgtatag 660
gactctttat cttgagctgt ggtatTTTTT ttttgttttt gtcttttaaa ttaagcctcg 720
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aaa 783

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<210> 52
<211> 808
<212> PRT
<213> Homo Sapiens

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<400> 52

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 Pro Arg Ala Pro Pro Ser Phe Pro Pro Pro Ala Ala Ser Arg Gly Gly
 20 25 30
 Leu Gly Gly Thr Arg Ser Phe Arg Pro His Arg Gly Ala Glu Ser Pro
 35 40 45
 Arg Pro Gly Arg Asp Arg Asp Gly Val Arg Val Pro Met Ala Ser Ser
 50 55 60
 Arg Cys Pro Ala Pro Arg Gly Cys Arg Cys Leu Pro Gly Ala Ser Leu
 65 70 75 80
 Ala Trp Leu Gly Thr Val Leu Leu Leu Leu Ala Asp Trp Val Leu Leu
 85 90 95
 Arg Thr Ala Leu Pro Arg Ile Phe Ser Leu Leu Val Pro Thr Ala Leu
 100 105 110
 Pro Leu Leu Arg Val Trp Ala Val Gly Leu Ser Arg Trp Ala Val Leu
 115 120 125
 Trp Leu Gly Ala Cys Gly Val Leu Arg Ala Thr Val Gly Ser Lys Ser
 130 135 140
 Glu Asn Ala Gly Ala Gln Gly Trp Leu Ala Ala Leu Lys Pro Leu Ala
 145 150 155 160
 Ala Ala Leu Gly Leu Ala Leu Pro Gly Leu Ala Leu Phe Arg Glu Leu
 165 170 175
 Ile Ser Trp Gly Ala Pro Gly Ser Ala Asp Ser Thr Arg Leu Leu His
 180 185 190
 Trp Gly Ser His Pro Thr Ala Phe Val Val Ser Tyr Ala Ala Ala Leu
 195 200 205
 Pro Ala Ala Ala Leu Trp His Lys Leu Gly Ser Leu Trp Val Pro Gly
 210 215 220
 Gly Gln Gly Gly Ser Gly Asn Pro Val Arg Arg Leu Leu Gly Cys Leu
 225 230 235 240
 Gly Ser Glu Thr Arg Arg Leu Ser Leu Phe Leu Val Leu Val Val Leu
 245 250 255
 Ser Ser Leu Gly Glu Met Ala Ile Pro Phe Phe Thr Gly Arg Leu Thr
 260 265 270
 Asp Trp Ile Leu Gln Asp Gly Ser Ala Asp Thr Phe Thr Arg Asn Leu
 275 280 285
 Thr Leu Met Ser Ile Leu Thr Ile Ala Ser Ala Val Leu Glu Phe Val
 290 295 300
 Gly Asp Gly Ile Tyr Asn Asn Thr Met Gly His Val His Ser His Leu
 305 310 315 320

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Gln Gly Glu Val Phe Gly Ala Val Leu Arg Gln Glu Thr Glu Phe Phe
 325 330 335
 Gln Gln Asn Gln Thr Gly Asn Ile Met Ser Arg Val Thr Glu Asp Thr
 340 345 350
 Ser Thr Leu Ser Asp Ser Leu Ser Glu Asn Leu Ser Leu Phe Leu Trp
 355 360 365
 Tyr Leu Val Arg Gly Leu Cys Leu Leu Gly Ile Met Leu Trp Gly Ser
 370 375 380
 Val Ser Leu Thr Met Val Thr Leu Ile Thr Leu Pro Leu Leu Phe Leu
 385 390 395 400
 Leu Pro Lys Lys Val Gly Lys Trp Tyr Gln Leu Leu Glu Val Gln Val
 405 410 415
 Arg Glu Ser Leu Ala Lys Ser Ser Gln Val Ala Ile Glu Ala Leu Ser
 420 425 430
 Ala Met Pro Thr Val Arg Ser Phe Ala Asn Glu Glu Gly Glu Ala Gln
 435 440 445
 Lys Phe Arg Glu Lys Leu Gln Glu Ile Lys Thr Leu Asn Gln Lys Glu
 450 455 460
 Ala Val Ala Tyr Ala Val Asn Ser Trp Thr Thr Ser Ile Ser Gly Met
 465 470 475 480
 Leu Leu Lys Val Gly Ile Leu Tyr Ile Gly Gly Gln Leu Val Thr Ser
 485 490 495
 Gly Ala Val Ser Ser Gly Asn Leu Val Thr Phe Val Leu Tyr Gln Met
 500 505 510
 Gln Phe Thr Gln Ala Val Glu Val Leu Leu Ser Ile Tyr Pro Arg Val
 515 520 525
 Gln Lys Ala Val Gly Ser Ser Glu Lys Ile Phe Glu Tyr Leu Asp Arg
 530 535 540
 Thr Pro Arg Cys Pro Pro Ser Gly Leu Leu Thr Pro Leu His Leu Glu
 545 550 555 560
 Gly Leu Val Gln Phe Gln Asp Val Ser Phe Ala Tyr Pro Asn Arg Pro
 565 570 575
 Asp Val Leu Val Leu Gln Gly Leu Thr Phe Thr Leu Arg Pro Gly Glu
 580 585 590
 Val Thr Ala Leu Val Gly Pro Asn Gly Ser Gly Lys Ser Thr Val Ala
 595 600 605
 Ala Leu Leu Gln Asn Leu Tyr Gln Pro Thr Gly Gly Gln Leu Leu Leu
 610 615 620
 Asp Gly Lys Pro Leu Pro Gln Tyr Glu His Arg Tyr Leu His Arg Gln
 625 630 635 640

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Val Ala Ala Val Gly Gln Glu Pro Gln Val Phe Gly Arg Ser Leu Gln
 645 650 655
 Glu Asn Ile Ala Tyr Gly Leu Thr Gln Lys Pro Thr Met Glu Glu Ile
 660 665 670
 Thr Ala Ala Ala Val Lys Ser Gly Ala His Ser Phe Ile Ser Gly Leu
 675 680 685
 Pro Gln Gly Tyr Asp Thr Glu Val Asp Glu Ala Gly Ser Gln Leu Ser
 690 695 700
 Gly Gly Gln Arg Gln Ala Val Ala Leu Ala Arg Ala Leu Ile Arg Lys
 705 710 715 720
 Pro Cys Val Leu Ile Leu Asp Asp Ala Thr Ser Ala Leu Asp Ala Asn
 725 730 735
 Ser Gln Leu Gln Val Glu Gln Leu Leu Tyr Glu Ser Pro Glu Arg Tyr
 740 745 750
 Ser Arg Ser Val Leu Leu Ile Thr Gln His Leu Ser Leu Val Glu Gln
 755 760 765
 Ala Asp His Ile Leu Phe Leu Glu Gly Gly Ala Ile Arg Glu Gly Gly
 770 775 780
 Thr His Gln Gln Leu Met Glu Lys Lys Gly Cys Tyr Trp Ala Met Val
 785 790 795 800
 Gln Ala Pro Ala Asp Ala Pro Glu
 805

<210> 53
 <211> 377
 <212> PRT
 <213> Homo Sapiens

<400> 53

Met Cys Glu Glu Glu Asp Ser Thr Ala Leu Val Cys Asp Asn Gly Ser
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 Gly Leu Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val
 20 25 30
 Phe Pro Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly
 35 40 45
 Met Gly Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg
 50 55 60
 Gly Ile Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Ile Thr Asn
 65 70 75 80
 Trp Asp Asp Met Glu Lys Ile Trp His His Ser Phe Tyr Asn Glu Leu
 85 90 95
 Arg Val Ala Pro Glu Glu His Pro Thr Leu Leu Thr Glu Ala Pro Leu
 100 105 110

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Asn Pro Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr
 115 120 125
 Phe Asn Val Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu
 130 135 140
 Tyr Ala Ser Gly Arg Thr Thr Gly Ile Val Leu Asp Ser Gly Asp Gly
 145 150 155 160
 Val Thr His Asn Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala
 165 170 175
 Ile Met Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met
 180 185 190
 Lys Ile Leu Thr Glu Arg Gly Tyr Ser Phe Val Thr Thr Ala Glu Arg
 195 200 205
 Glu Ile Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp
 210 215 220
 Phe Glu Asn Glu Met Ala Thr Ala Ala Ser Ser Ser Ser Leu Glu Lys
 225 230 235 240
 Ser Tyr Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg
 245 250 255
 Phe Arg Cys Pro Glu Thr Leu Phe Gln Pro Ser Phe Ile Gly Met Glu
 260 265 270
 Ser Ala Gly Ile His Glu Thr Thr Tyr Asn Ser Ile Met Lys Cys Asp
 275 280 285
 Ile Asp Ile Arg Lys Asp Leu Tyr Ala Asn Asn Val Leu Ser Gly Gly
 290 295 300
 Thr Thr Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr
 305 310 315 320
 Ala Leu Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu
 325 330 335
 Arg Lys Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser
 340 345 350
 Thr Phe Gln Gln Met Trp Ile Ser Lys Gln Glu Tyr Asp Glu Ala Gly
 355 360 365
 Pro Ser Ile Val His Arg Lys Cys Phe
 370 375

<210> 54
 <211> 334
 <212> PRT
 <213> Homo Sapiens

<400> 54

Met Glu Ala Ala His Phe Phe Glu Gly Thr Glu Lys Leu Leu Glu Val

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			20					25					30						
Arg	Thr	Ile	Pro	Arg	Ser	Glu	Trp	Asp	Ile	Leu	Leu	Lys	Asp	Val	Gln				
		35					40					45							
Cys	Ser	Ile	Ile	Ser	Val	Thr	Lys	Thr	Asp	Lys	Gln	Glu	Ala	Tyr	Val				
	50					55					60								
Leu	Ser	Glu	Ser	Ser	Met	Phe	Val	Ser	Lys	Arg	Arg	Phe	Ile	Leu	Lys				
65					70					75					80				
Thr	Cys	Gly	Thr	Thr	Leu	Leu	Leu	Lys	Ala	Leu	Val	Pro	Leu	Leu	Lys				
				85					90					95					
Leu	Ala	Arg	Asp	Tyr	Ser	Gly	Phe	Asp	Ser	Ile	Gln	Ser	Phe	Phe	Tyr				
			100					105					110						
Ser	Arg	Lys	Asn	Phe	Met	Lys	Pro	Ser	His	Gln	Gly	Tyr	Pro	His	Arg				
		115					120					125							
Asn	Phe	Gln	Glu	Glu	Ile	Glu	Phe	Leu	Asn	Ala	Ile	Phe	Pro	Asn	Gly				
	130					135					140								
Ala	Gly	Tyr	Cys	Met	Gly	Arg	Met	Asn	Ser	Asp	Cys	Trp	Tyr	Leu	Tyr				
145					150					155					160				
Thr	Leu	Asp	Phe	Pro	Glu	Ser	Arg	Val	Ile	Ser	Gln	Pro	Asp	Gln	Thr				
				165					170					175					
Leu	Glu	Ile	Leu	Met	Ser	Glu	Leu	Asp	Pro	Ala	Val	Met	Asp	Gln	Phe				
			180					185					190						
Tyr	Met	Lys	Asp	Gly	Val	Thr	Ala	Lys	Asp	Val	Thr	Arg	Glu	Ser	Gly				
	195						200					205							
Ile	Arg	Asp	Leu	Ile	Pro	Gly	Ser	Val	Ile	Asp	Ala	Thr	Met	Phe	Asn				
	210					215					220								
Pro	Cys	Gly	Tyr	Ser	Met	Asn	Gly	Met	Lys	Ser	Asp	Gly	Thr	Tyr	Trp				
225					230					235					240				
Thr	Ile	His	Ile	Thr	Pro	Glu	Pro	Glu	Phe	Ser	Tyr	Val	Ser	Phe	Glu				
				245					250					255					
Thr	Asn	Leu	Ser	Gln	Thr	Ser	Tyr	Asp	Asp	Leu	Ile	Arg	Lys	Val	Val				
			260					265					270						
Glu	Val	Phe	Lys	Pro	Gly	Lys	Phe	Val	Thr	Thr	Leu	Phe	Val	Asn	Gln				
		275					280					285							
Ser	Ser	Lys	Cys	Arg	Thr	Val	Leu	Ala	Ser	Pro	Gln	Lys	Ile	Glu	Gly				
	290					295					300								
Phe	Lys	Arg	Leu	Asp	Cys	Gln	Ser	Ala	Met	Phe	Asn	Asp	Tyr	Asn	Phe				
305					310					315				320					
Val	Phe	Thr	Ser	Phe	Ala	Lys	Lys	Gln	Gln	Gln	Gln	Gln	Gln	Ser					

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330

<210> 55
 <211> 76
 <212> PRT
 <213> Homo Sapiens

<400> 55

Met Ala Ser Lys Gly Leu Gln Asp Leu Lys Gln Gln Val Glu Gly Thr
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 Ala Gln Glu Ala Val Ser Ala Ala Gly Ala Ala Ala Gln Gln Val Val
 20 25 30
 Asp Gln Ala Thr Glu Ala Gly Gln Lys Ala Met Asp Gln Leu Ala Lys
 35 40 45
 Thr Thr Gln Glu Thr Ile Asp Lys Thr Ala Asn Gln Ala Ser Asp Thr
 50 55 60
 Phe Ser Gly Ile Gly Lys Lys Phe Gly Leu Leu Lys
 65 70 75

<210> 56
 <211> 395
 <212> PRT
 <213> Homo Sapiens

<400> 56

Met Pro Gly Arg Ser Cys Val Ala Leu Val Leu Leu Ala Ala Ala Val
 1 5 10 15
 Ser Cys Ala Val Ala Gln His Ala Pro Pro Trp Thr Glu Asp Cys Arg
 20 25 30
 Lys Ser Thr Tyr Pro Pro Ser Gly Pro Thr Tyr Arg Gly Ala Val Pro
 35 40 45
 Trp Tyr Thr Ile Asn Leu Asp Leu Pro Pro Tyr Lys Arg Trp His Glu
 50 55 60
 Leu Met Leu Asp Lys Ala Pro Met Leu Lys Val Ile Val Asn Ser Leu
 65 70 75 80
 Lys Asn Met Ile Asn Thr Phe Val Pro Ser Gly Lys Val Met Gln Val
 85 90 95
 Val Asp Glu Lys Leu Pro Gly Leu Leu Gly Asn Phe Pro Gly Pro Phe
 100 105 110
 Glu Glu Glu Met Lys Gly Ile Ala Ala Val Thr Asp Ile Pro Leu Gly
 115 120 125
 Glu Ile Ile Ser Phe Asn Ile Phe Tyr Glu Leu Phe Thr Ile Cys Thr
 130 135 140
 Ser Ile Val Ala Glu Asp Lys Lys Gly His Leu Ile His Gly Arg Asn
 145 150 155 160

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Met Asp Phe Gly Val Phe Leu Gly Trp Asn Ile Asn Asn Asp Thr Trp
165 170 175

Val Ile Thr Glu Gln Leu Lys Pro Leu Thr Val Asn Leu Asp Phe Gln
180 185 190

Arg Asn Asn Lys Thr Val Phe Lys Ala Ser Ser Phe Ala Gly Tyr Val
195 200 205

Gly Met Leu Thr Gly Phe Lys Pro Gly Leu Phe Ser Leu Thr Leu Asn
210 215 220

Glu Arg Phe Ser Ile Asn Gly Gly Tyr Leu Gly Ile Leu Glu Trp Ile
225 230 235 240

Leu Gly Lys Lys Asp Ala Met Trp Ile Gly Phe Leu Thr Arg Thr Val
245 250 255

Leu Glu Asn Ser Thr Ser Tyr Glu Glu Ala Lys Asn Leu Leu Thr Lys
260 265 270

Thr Lys Ile Leu Ala Pro Ala Tyr Phe Ile Leu Gly Gly Asn Gln Ser
275 280 285

Gly Glu Gly Cys Val Ile Thr Arg Asp Arg Lys Glu Ser Leu Asp Val
290 295 300

Tyr Glu Leu Asp Ala Lys Gln Gly Arg Trp Tyr Val Val Gln Thr Asn
305 310 315 320

Tyr Asp Arg Trp Lys His Pro Phe Phe Leu Asp Asp Arg Arg Thr Pro
325 330 335

Ala Lys Met Cys Leu Asn Arg Thr Ser Gln Glu Asn Ile Ser Phe Glu
340 345 350

Thr Met Tyr Asp Val Leu Ser Thr Lys Pro Val Leu Asn Lys Leu Thr
355 360 365

Val Tyr Thr Thr Leu Ile Asp Val Thr Lys Gly Gln Phe Glu Thr Tyr
370 375 380

Leu Arg Asp Cys Pro Asp Pro Cys Ile Gly Trp
385 390 395

<210> 57
<211> 777
<212> PRT
<213> Homo Sapiens

<400> 57

Met Pro Asp Asn Arg Gln Pro Arg Asn Arg Gln Pro Arg Ile Arg Ser
1 5 10 15

Gly Asn Glu Pro Arg Ser Ala Pro Ala Met Glu Pro Asp Gly Arg Gly
20 25 30

Ala Trp Ala His Ser Arg Ala Ala Leu Asp Arg Leu Glu Lys Leu Leu

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35					40					45					
Arg	Cys	Ser	Arg	Cys	Thr	Asn	Ile	Leu	Arg	Glu	Pro	Val	Cys	Leu	Gly
50						55					60				
Gly	Cys	Glu	His	Ile	Phe	Cys	Ser	Asn	Cys	Val	Ser	Asp	Cys	Ile	Gly
65					70					75					80
Thr	Gly	Cys	Pro	Val	Cys	Tyr	Thr	Pro	Ala	Trp	Ile	Gln	Asp	Leu	Lys
				85					90					95	
Ile	Asn	Arg	Gln	Leu	Asp	Ser	Met	Ile	Gln	Leu	Cys	Ser	Lys	Leu	Arg
			100					105					110		
Asn	Leu	Leu	His	Asp	Asn	Glu	Leu	Ser	Asp	Leu	Lys	Glu	Asp	Lys	Pro
			115				120					125			
Arg	Lys	Ser	Leu	Phe	Asn	Asp	Ala	Gly	Asn	Lys	Lys	Asn	Ser	Ile	Lys
	130					135					140				
Met	Trp	Phe	Ser	Pro	Arg	Ser	Lys	Lys	Val	Arg	Tyr	Val	Val	Ser	Lys
145					150					155					160
Ala	Ser	Val	Gln	Thr	Gln	Pro	Ala	Ile	Lys	Lys	Asp	Ala	Ser	Ala	Gln
				165					170					175	
Gln	Asp	Ser	Tyr	Glu	Phe	Val	Ser	Pro	Ser	Pro	Pro	Ala	Asp	Val	Ser
			180					185					190		
Glu	Arg	Ala	Lys	Lys	Ala	Ser	Ala	Arg	Ser	Gly	Lys	Lys	Gln	Lys	Lys
		195					200					205			
Lys	Thr	Leu	Ala	Glu	Ile	Asn	Gln	Lys	Trp	Asn	Leu	Glu	Ala	Glu	Lys
	210					215					220				
Glu	Asp	Gly	Glu	Phe	Asp	Ser	Lys	Glu	Glu	Ser	Lys	Gln	Lys	Leu	Val
225					230					235					240
Ser	Phe	Cys	Ser	Gln	Pro	Ser	Val	Ile	Ser	Ser	Pro	Gln	Ile	Asn	Gly
				245					250					255	
Glu	Ile	Asp	Leu	Leu	Ala	Ser	Gly	Ser	Leu	Thr	Glu	Ser	Glu	Cys	Phe
			260					265					270		
Gly	Ser	Leu	Thr	Glu	Val	Ser	Leu	Pro	Leu	Ala	Glu	Gln	Ile	Glu	Ser
		275					280					285			
Pro	Asp	Thr	Lys	Ser	Arg	Asn	Glu	Val	Val	Thr	Pro	Glu	Lys	Val	Cys
	290					295					300				
Lys	Asn	Tyr	Leu	Thr	Ser	Lys	Lys	Ser	Leu	Pro	Leu	Glu	Asn	Asn	Gly
305					310					315					320
Lys	Arg	Gly	His	His	Asn	Arg	Leu	Ser	Ser	Pro	Ile	Ser	Lys	Arg	Cys
				325					330					335	
Arg	Thr	Ser	Ile	Leu	Ser	Thr	Ser	Gly	Asp	Phe	Val	Lys	Gln	Thr	Val
			340					345					350		
Pro	Ser	Glu	Asn	Ile	Pro	Leu	Pro	Glu	Cys	Ser	Ser	Pro	Pro	Ser	Cys

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355					360					365					
Lys	Arg	Lys	Val	Gly	Gly	Thr	Ser	Gly	Arg	Lys	Asn	Ser	Asn	Met	Ser
370					375					380					
Asp	Glu	Phe	Ile	Ser	Leu	Ser	Pro	Gly	Thr	Pro	Pro	Ser	Thr	Leu	Ser
385					390					395					400
Ser	Ser	Ser	Tyr	Arg	Gln	Val	Met	Ser	Ser	Pro	Ser	Ala	Met	Lys	Leu
				405					410					415	
Leu	Pro	Asn	Met	Ala	Val	Lys	Arg	Asn	His	Arg	Gly	Glu	Thr	Leu	Leu
			420					425					430		
His	Ile	Ala	Ser	Ile	Lys	Gly	Asp	Ile	Pro	Ser	Val	Glu	Tyr	Leu	Leu
		435					440					445			
Gln	Asn	Gly	Ser	Asp	Pro	Asn	Val	Lys	Asp	His	Ala	Gly	Trp	Thr	Pro
	450					455					460				
Leu	His	Glu	Ala	Cys	Asn	His	Gly	His	Leu	Lys	Val	Val	Glu	Leu	Leu
465					470					475					480
Leu	Gln	His	Lys	Ala	Leu	Val	Asn	Thr	Thr	Gly	Tyr	Gln	Asn	Asp	Ser
			485						490					495	
Pro	Leu	His	Asp	Ala	Ala	Lys	Asn	Gly	His	Val	Asp	Ile	Val	Lys	Leu
			500					505					510		
Leu	Leu	Ser	Tyr	Gly	Ala	Ser	Arg	Asn	Ala	Val	Asn	Ile	Phe	Gly	Leu
		515					520					525			
Arg	Pro	Val	Asp	Tyr	Thr	Asp	Asp	Glu	Ser	Met	Lys	Ser	Leu	Leu	Leu
	530					535					540				
Leu	Pro	Glu	Lys	Asn	Glu	Ser	Ser	Ser	Ala	Ser	His	Cys	Ser	Val	Met
545					550					555					560
Asn	Thr	Gly	Gln	Arg	Arg	Asp	Gly	Pro	Leu	Val	Leu	Ile	Gly	Ser	Gly
			565					570					575		
Leu	Ser	Ser	Glu	Gln	Gln	Lys	Met	Leu	Ser	Glu	Leu	Ala	Val	Ile	Leu
			580				585					590			
Lys	Ala	Lys	Lys	Tyr	Thr	Glu	Phe	Asp	Ser	Thr	Val	Thr	His	Val	Val
	595						600					605			
Val	Pro	Gly	Asp	Ala	Val	Gln	Ser	Thr	Leu	Lys	Cys	Met	Leu	Gly	Ile
	610					615					620				
Leu	Asn	Gly	Cys	Trp	Ile	Leu	Lys	Phe	Glu	Trp	Val	Lys	Ala	Cys	Leu
625					630					635					640
Arg	Arg	Lys	Val	Cys	Glu	Gln	Glu	Glu	Lys	Tyr	Glu	Ile	Pro	Glu	Gly
			645						650					655	
Pro	Arg	Arg	Ser	Arg	Leu	Asn	Arg	Glu	Gln	Leu	Leu	Pro	Lys	Leu	Phe
			660					665					670		
Asp	Gly	Cys	Tyr	Phe	Tyr	Leu	Trp	Gly	Thr	Phe	Lys	His	His	Pro	Lys

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675	680	685
Asp Asn Leu Ile Lys Leu Val Thr Ala Gly Gly Gly Gln Ile Leu Ser		
690	695	700
Arg Lys Pro Lys Pro Asp Ser Asp Val Thr Gln Thr Ile Asn Thr Val		
705	710	715
Ala Tyr His Ala Arg Pro Asp Ser Asp Gln Arg Phe Cys Thr Gln Tyr		
	725	730
		735
Ile Ile Tyr Glu Asp Leu Cys Asn Tyr His Pro Glu Arg Val Arg Gln		
	740	745
		750
Gly Lys Val Trp Lys Ala Pro Ser Ser Trp Phe Ile Asp Cys Val Met		
	755	760
		765
Ser Phe Glu Leu Leu Pro Leu Asp Ser		
770	775	

<210> 58
 <211> 323
 <212> PRT
 <213> Homo Sapiens

<400> 58

Met Tyr His Asn Ser Ser Gln Lys Arg His Trp Thr Phe Ser Ser Glu		
1	5	10
		15
Glu Gln Leu Ala Arg Leu Arg Ala Asp Ala Asn Arg Lys Phe Arg Cys		
	20	25
		30
Lys Ala Val Ala Asn Gly Lys Val Leu Pro Asn Asp Pro Val Phe Leu		
	35	40
		45
Glu Pro His Glu Glu Met Thr Leu Cys Lys Tyr Tyr Glu Lys Arg Leu		
	50	55
		60
Leu Glu Phe Cys Ser Val Phe Lys Pro Ala Met Pro Arg Ser Val Val		
65	70	75
		80
Gly Thr Ala Cys Met Tyr Phe Lys Arg Phe Tyr Leu Asn Asn Ser Val		
	85	90
		95
Met Glu Tyr His Pro Arg Ile Ile Met Leu Thr Cys Ala Phe Leu Ala		
	100	105
		110
Cys Lys Val Asp Glu Phe Asn Val Ser Ser Pro Gln Phe Val Gly Asn		
	115	120
		125
Leu Arg Glu Ser Pro Leu Gly Gln Glu Lys Ala Leu Glu Gln Ile Leu		
	130	135
		140
Glu Tyr Glu Leu Leu Leu Ile Gln Gln Leu Asn Phe His Leu Ile Val		
145	150	155
		160
His Asn Pro Tyr Arg Pro Phe Glu Gly Phe Leu Ile Asp Leu Lys Thr		
	165	170
		175

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Arg Tyr Pro Ile Leu Glu Asn Pro Glu Ile Leu Arg Lys Thr Ala Asp
 180 185 190
 Asp Phe Leu Asn Arg Ile Ala Leu Thr Asp Ala Tyr Leu Leu Tyr Thr
 195 200 205
 Pro Ser Gln Ile Ala Leu Thr Ala Ile Leu Ser Ser Ala Ser Arg Ala
 210 215 220
 Gly Ile Thr Met Glu Ser Tyr Leu Ser Glu Ser Leu Met Leu Lys Glu
 225 230 235 240
 Asn Arg Thr Cys Leu Ser Gln Leu Leu Asp Ile Met Lys Ser Met Arg
 245 250 255
 Asn Leu Val Lys Lys Tyr Glu Pro Pro Arg Ser Glu Glu Val Ala Val
 260 265 270
 Leu Lys Gln Lys Leu Glu Arg Cys His Ser Ala Glu Leu Ala Leu Asn
 275 280 285
 Val Ile Thr Lys Lys Arg Lys Gly Tyr Glu Asp Asp Asp Tyr Val Ser
 290 295 300
 Lys Lys Ser Lys His Glu Glu Glu Glu Trp Thr Asp Asp Asp Leu Val
 305 310 315 320
 Glu Ser Leu

<210> 59
 <211> 217
 <212> PRT
 <213> Homo Sapiens

<400> 59

Met Ala Ser Leu Ser Leu Ala Pro Val Asn Ile Phe Lys Ala Gly Ala
 1 5 10 15
 Asp Glu Glu Arg Ala Glu Thr Ala Arg Leu Thr Ser Phe Ile Gly Ala
 20 25 30
 Ile Ala Ile Gly Asp Leu Val Lys Ser Thr Leu Gly Pro Lys Gly Met
 35 40 45
 Asp Lys Ile Leu Leu Ser Ser Gly Arg Asp Ala Ser Leu Met Val Thr
 50 55 60
 Asn Asp Gly Ala Thr Ile Leu Lys Asn Ile Gly Val Asp Asn Pro Ala
 65 70 75 80
 Ala Lys Val Leu Val Asp Met Ser Arg Val Gln Asp Asp Glu Val Gly
 85 90 95
 Asp Gly Thr Thr Ser Val Thr Val Leu Ala Ala Glu Leu Leu Arg Glu
 100 105 110
 Ala Glu Ser Leu Ile Ala Lys Lys Ile His Pro Gln Thr Ile Ile Ala
 115 120 125

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Gly Trp Arg Glu Ala Thr Lys Ala Ala Arg Glu Ala Leu Leu Ser Ser
 130 135 140

Ala Val Asp His Gly Ser Asp Glu Val Lys Phe Arg Gln Asp Leu Met
 145 150 155 160

Asn Ile Ala Gly Thr Thr Leu Ser Ser Lys Leu Leu Thr His His Lys
 165 170 175

Asp His Phe Thr Lys Leu Ala Val Glu Ala Val Leu Arg Leu Lys Gly
 180 185 190

Ser Gly Asn Leu Glu Ala Ile His Ile Ile Lys Lys Leu Gly Gly Ser
 195 200 205

Leu Ala Asp Ser Tyr Leu Asp Glu Gly
 210 215

<210> 60
 <211> 499
 <212> PRT
 <213> Homo Sapiens

<400> 60

Met Ala Gln Phe Ala Phe Glu Ser Asp Leu His Ser Leu Leu Gln Leu
 1 5 10 15

Asp Ala Pro Ile Pro Asn Ala Pro Pro Ala Arg Trp Gln Arg Lys Ala
 20 25 30

Lys Glu Ala Ala Gly Pro Ala Pro Ser Pro Met Arg Ala Ala Asn Arg
 35 40 45

Ser His Ser Ala Gly Arg Thr Pro Gly Arg Thr Pro Gly Lys Ser Ser
 50 55 60

Ser Lys Val Gln Thr Thr Pro Ser Lys Pro Gly Gly Asp Arg Tyr Ile
 65 70 75 80

Pro His Arg Ser Ala Ala Gln Met Glu Val Ala Ser Phe Leu Leu Ser
 85 90 95

Lys Glu Asn Gln Ser Glu Asn Ser Gln Thr Pro Thr Lys Lys Glu His
 100 105 110

Gln Lys Ala Trp Ala Leu Asn Leu Asn Gly Phe Asp Val Glu Glu Ala
 115 120 125

Lys Ile Leu Arg Leu Ser Gly Lys Pro Gln Asn Ala Pro Glu Gly Tyr
 130 135 140

Gln Asn Arg Leu Lys Val Leu Tyr Ser Gln Lys Ala Thr Pro Gly Ser
 145 150 155 160

Ser Arg Lys Thr Cys Arg Tyr Ile Pro Ser Leu Pro Asp Arg Ile Leu
 165 170 175

Asp Ala Pro Glu Ile Arg Asn Asp Tyr Tyr Leu Asn Leu Val Asp Trp

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180					185					190					
Ser	Ser	Gly	Asn	Val	Leu	Ala	Val	Ala	Leu	Asp	Asn	Ser	Val	Tyr	Leu
		195					200					205			
Trp	Ser	Ala	Ser	Ser	Gly	Asp	Ile	Leu	Gln	Leu	Leu	Gln	Met	Glu	Gln
		210				215					220				
Pro	Gly	Glu	Tyr	Ile	Ser	Ser	Val	Ala	Trp	Ile	Lys	Glu	Gly	Asn	Tyr
225					230					235					240
Leu	Ala	Val	Gly	Thr	Ser	Ser	Ala	Glu	Val	Gln	Leu	Trp	Asp	Val	Gln
				245					250					255	
Gln	Gln	Lys	Arg	Leu	Arg	Asn	Met	Thr	Ser	His	Ser	Ala	Arg	Val	Gly
			260					265					270		
Ser	Leu	Ser	Trp	Asn	Ser	Tyr	Ile	Leu	Ser	Ser	Gly	Ser	Arg	Ser	Gly
		275					280					285			
His	Ile	His	His	His	Asp	Val	Arg	Val	Ala	Glu	His	His	Val	Ala	Thr
	290					295					300				
Leu	Ser	Gly	His	Ser	Gln	Glu	Val	Cys	Gly	Leu	Arg	Trp	Ala	Pro	Asp
305					310					315					320
Gly	Arg	His	Leu	Ala	Ser	Gly	Gly	Asn	Asp	Asn	Leu	Val	Asn	Val	Trp
				325					330					335	
Pro	Ser	Ala	Pro	Gly	Glu	Gly	Gly	Trp	Val	Pro	Leu	Gln	Thr	Phe	Thr
			340					345					350		
Gln	His	Gln	Gly	Ala	Val	Lys	Ala	Val	Ala	Trp	Cys	Pro	Trp	Gln	Ser
		355					360					365			
Asn	Val	Leu	Ala	Thr	Gly	Gly	Gly	Thr	Ser	Asp	Arg	His	Ile	Arg	Ile
	370					375					380				
Trp	Asn	Val	Cys	Ser	Gly	Ala	Cys	Leu	Ser	Ala	Val	Asp	Ala	His	Ser
385					390					395					400
Gln	Val	Cys	Ser	Ile	Leu	Trp	Ser	Pro	His	Tyr	Lys	Glu	Leu	Ile	Ser
				405					410					415	
Gly	His	Gly	Phe	Ala	Gln	Asn	Gln	Leu	Val	Ile	Trp	Lys	Tyr	Pro	Thr
			420					425					430		
Met	Ala	Lys	Val	Ala	Glu	Leu	Lys	Gly	His	Thr	Ser	Arg	Val	Leu	Ser
		435					440					445			
Leu	Thr	Met	Ser	Pro	Asp	Gly	Ala	Thr	Val	Ala	Ser	Ala	Ala	Ala	Asp
	450					455					460				
Glu	Thr	Leu	Arg	Leu	Trp	Arg	Cys	Phe	Glu	Leu	Asp	Pro	Ala	Arg	Arg
465					470					475					480
Arg	Glu	Arg	Glu	Lys	Ala	Ser	Ala	Ala	Lys	Ser	Ser	Leu	Ile	His	Gln
				485					490					495	
Gly	Ile	Arg													

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<210> 61
 <211> 298
 <212> PRT
 <213> Homo Sapiens

<400> 61

Ile	Ala	Ala	Ala	Pro	Glu	Leu	Leu	Glu	Arg	Ser	Gly	Ser	Pro	Gly	Gly	1	5	10	15
Gly	Gly	Gly	Ala	Glu	Glu	Glu	Ala	Gly	Gly	Gly	Pro	Gly	Gly	Ser	Pro	20	25	30	
Pro	Asp	Gly	Ala	Arg	Pro	Gly	Pro	Ser	Arg	Glu	Leu	Ala	Val	Val	Ala	35	40	45	
Arg	Pro	Arg	Ala	Ala	Pro	Thr	Pro	Gly	Pro	Ser	Ala	Ala	Ala	Met	Ala	50	55	60	
Arg	Pro	Leu	Val	Pro	Ser	Ser	Gln	Lys	Ala	Leu	Leu	Leu	Glu	Leu	Lys	65	70	75	80
Gly	Leu	Gln	Glu	Glu	Pro	Val	Glu	Gly	Phe	Arg	Val	Thr	Leu	Val	Asp	85	90	95	
Glu	Gly	Asp	Leu	Tyr	Asn	Trp	Glu	Val	Ala	Ile	Phe	Gly	Pro	Pro	Asn	100	105	110	
Thr	Tyr	Tyr	Glu	Gly	Gly	Tyr	Phe	Lys	Ala	Arg	Leu	Lys	Phe	Pro	Ile	115	120	125	
Asp	Tyr	Pro	Tyr	Ser	Pro	Pro	Ala	Phe	Arg	Phe	Leu	Thr	Lys	Met	Trp	130	135	140	
His	Pro	Asn	Ile	Tyr	Glu	Thr	Gly	Asp	Val	Cys	Ile	Ser	Ile	Leu	His	145	150	155	160
Pro	Pro	Val	Asp	Asp	Pro	Gln	Ser	Gly	Glu	Leu	Pro	Ser	Glu	Arg	Trp	165	170	175	
Asn	Pro	Thr	Gln	Asn	Val	Arg	Thr	Ile	Leu	Leu	Ser	Val	Ile	Ser	Leu	180	185	190	
Leu	Asn	Glu	Pro	Asn	Thr	Phe	Ser	Pro	Ala	Asn	Val	Asp	Ala	Ser	Val	195	200	205	
Met	Tyr	Arg	Lys	Trp	Lys	Glu	Ser	Lys	Gly	Lys	Asp	Arg	Glu	Tyr	Thr	210	215	220	
Asp	Ile	Ile	Arg	Lys	Gln	Val	Leu	Gly	Thr	Lys	Val	Asp	Ala	Glu	Arg	225	230	235	240
Asp	Gly	Val	Lys	Val	Pro	Thr	Thr	Leu	Ala	Glu	Tyr	Cys	Val	Lys	Thr	245	250	255	
Lys	Ala	Pro	Ala	Pro	Asp	Glu	Gly	Ser	Asp	Leu	Phe	Tyr	Asp	Asp	Tyr	260	265	270	

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Tyr Glu Asp Gly Glu Val Glu Glu Glu Ala Asp Ser Cys Phe Gly Asp
 275 280 285

Asp Glu Asp Asp Ser Gly Thr Glu Glu Ser
 290 295

<210> 62
 <211> 212
 <212> PRT
 <213> Homo Sapiens

<400> 62

Met Glu Pro Pro Ser Ser Ile Gln Thr Ser Glu Phe Asp Ser Ser Asp
 1 5 10 15

Glu Glu Pro Ile Glu Asp Glu Gln Thr Pro Ile His Ile Ser Trp Leu
 20 25 30

Ser Leu Ser Arg Val Asn Cys Ser Gln Phe Leu Gly Leu Cys Ala Leu
 35 40 45

Pro Gly Cys Lys Phe Lys Asp Val Arg Arg Asn Val Gln Lys Asp Thr
 50 55 60

Glu Glu Leu Lys Ser Cys Gly Ile Gln Asp Ile Phe Val Phe Cys Thr
 65 70 75 80

Arg Gly Glu Leu Ser Lys Tyr Arg Val Pro Asn Leu Leu Asp Leu Tyr
 85 90 95

Gln Gln Cys Gly Ile Ile Thr His His His Pro Ile Ala Asp Gly Gly
 100 105 110

Thr Pro Asp Ile Ala Ser Cys Cys Glu Ile Met Glu Glu Leu Thr Thr
 115 120 125

Cys Leu Lys Asn Tyr Arg Lys Thr Leu Ile His Cys Tyr Gly Gly Leu
 130 135 140

Gly Arg Ser Cys Leu Val Ala Ala Cys Leu Leu Leu Tyr Leu Ser Asp
 145 150 155 160

Thr Ile Ser Pro Glu Gln Ala Ile Asp Ser Leu Arg Asp Leu Arg Gly
 165 170 175

Ser Gly Ala Ile Gln Thr Ile Lys Gln Tyr Asn Tyr Leu His Glu Phe
 180 185 190

Arg Asp Lys Leu Ala Ala His Leu Ser Ser Arg Asp Ser Gln Ser Arg
 195 200 205

Ser Val Ser Arg
 210

<210> 63
 <211> 79
 <212> PRT
 <213> Homo Sapiens

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<400> 63

```

Met Ser His Lys Gln Ile Tyr Tyr Ser Asp Lys Tyr Asp Asp Glu Glu
1          5          10          15
Phe Glu Tyr Arg His Val Met Leu Pro Lys Asp Ile Ala Lys Leu Val
          20          25          30
Pro Lys Thr His Leu Met Ser Glu Ser Glu Trp Arg Asn Leu Gly Val
          35          40          45
Gln Gln Ser Gln Gly Trp Val His Tyr Met Ile His Glu Pro Glu Pro
          50          55          60
His Ile Leu Leu Phe Arg Arg Pro Leu Pro Lys Lys Pro Lys Lys
65          70          75

```

<210> 64

<211> 79

<212> PRT

<213> Homo Sapiens

<400> 64

```

Met Ala His Lys Gln Ile Tyr Tyr Ser Asp Lys Tyr Phe Asp Glu His
1          5          10          15
Tyr Glu Tyr Arg His Val Met Leu Pro Arg Glu Leu Ser Lys Gln Val
          20          25          30
Pro Lys Thr His Leu Met Ser Glu Glu Glu Trp Arg Arg Leu Gly Val
          35          40          45
Gln Gln Ser Leu Gly Trp Val His Tyr Met Ile His Glu Pro Glu Pro
          50          55          60
His Ile Leu Leu Phe Arg Arg Pro Leu Pro Lys Asp Gln Gln Lys
65          70          75

```

<210> 65

<211> 79

<212> PRT

<213> Homo Sapiens

<400> 65

```

Met Gln Ala Leu Arg Val Ser Gln Ala Leu Ile Arg Ser Phe Ser Ser
1          5          10          15
Thr Ala Arg Asn Arg Phe Gln Asn Arg Val Arg Glu Lys Gln Lys Leu
          20          25          30
Phe Gln Glu Asp Asn Asp Ile Pro Leu Tyr Leu Lys Gly Gly Ile Val
          35          40          45
Asp Asn Ile Leu Tyr Arg Val Thr Met Thr Leu Cys Leu Gly Gly Thr
          50          55          60
Val Tyr Ser Leu Tyr Ser Leu Gly Trp Ala Ser Phe Pro Arg Asn
65          70          75

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<210> 66

<211> 417

<212> PRT

<213> Homo Sapiens

<400> 66

```

Met Arg Leu Ile Leu Pro Val Gly Leu Ile Ala Thr Thr Leu Ala Ile
1           5           10           15

Ala Pro Val Arg Phe Asp Arg Glu Lys Val Phe Arg Val Lys Pro Gln
          20           25           30

Asp Glu Lys Gln Ala Asp Ile Ile Lys Asp Leu Ala Lys Thr Asn Glu
          35           40           45

Leu Asp Phe Trp Tyr Pro Gly Ala Thr His His Val Ala Ala Asn Met
          50           55           60

Met Val Asp Phe Arg Val Ser Glu Lys Glu Ser Gln Ala Ile Gln Ser
65           70           75           80

Ala Leu Asp Gln Asn Lys Met His Tyr Glu Ile Leu Ile His Asp Leu
          85           90           95

Gln Glu Glu Ile Glu Lys Gln Phe Asp Val Lys Glu Asp Ile Pro Gly
          100          105          110

Arg His Ser Tyr Ala Lys Tyr Asn Asn Trp Glu Lys Ile Val Ala Trp
          115          120          125

Thr Glu Lys Met Met Asp Lys Tyr Pro Glu Met Val Ser Arg Ile Lys
          130          135          140

Ile Gly Ser Thr Val Glu Asp Asn Pro Leu Tyr Val Leu Lys Ile Gly
145          150          155          160

Glu Lys Asn Glu Arg Arg Lys Ala Ile Phe Met Asp Cys Gly Ile His
          165          170          175

Ala Arg Glu Trp Val Ser Pro Ala Phe Cys Gln Trp Phe Val Tyr Gln
          180          185          190

Ala Thr Lys Thr Tyr Gly Arg Asn Lys Ile Met Thr Lys Leu Leu Asp
          195          200          205

Arg Met Asn Phe Tyr Ile Leu Pro Val Phe Asn Val Asp Gly Tyr Ile
          210          215          220

Trp Ser Trp Thr Lys Asn Arg Met Trp Arg Lys Asn Arg Ser Lys Asn
225          230          235          240

Gln Asn Ser Lys Cys Ile Gly Thr Asp Leu Asn Arg Asn Phe Asn Ala
          245          250          255

Ser Trp Asn Ser Ile Pro Asn Thr Asn Asp Pro Cys Ala Asp Asn Tyr
          260          265          270

Arg Gly Ser Ala Pro Glu Ser Glu Lys Glu Thr Lys Ala Val Thr Asn

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275	280	285
Phe Ile Arg Ser His Leu Asn Glu Ile Lys Val Tyr Ile Thr Phe His		
290	295	300
Ser Tyr Ser Gln Met Leu Leu Phe Pro Tyr Gly Tyr Thr Ser Lys Leu		
305	310	315
Pro Pro Asn His Glu Asp Leu Ala Lys Val Ala Lys Ile Gly Thr Asp		
	325	330
Val Leu Ser Thr Arg Tyr Glu Thr Arg Tyr Ile Tyr Gly Pro Ile Glu		
	340	345
Ser Thr Ile Tyr Pro Ile Ser Gly Ser Ser Leu Asp Trp Ala Tyr Asp		
	355	360
Leu Gly Ile Lys His Thr Phe Ala Phe Glu Leu Arg Asp Lys Gly Lys		
	370	375
Phe Gly Phe Leu Leu Pro Glu Ser Arg Ile Lys Pro Thr Cys Arg Glu		
385	390	395
Thr Met Leu Ala Val Lys Phe Ile Ala Lys Tyr Ile Leu Lys His Thr		
	405	410
		415

Ser

<210> 67
 <211> 476
 <212> PRT
 <213> Homo Sapiens

<400> 67

Met Ala Gly Arg Gly Gly Ser Ala Leu Leu Ala Leu Cys Gly Ala Leu	
1	5 10 15
Ala Ala Cys Gly Trp Leu Leu Gly Ala Glu Ala Gln Glu Pro Gly Ala	
	20 25 30
Pro Ala Ala Gly Met Arg Arg Arg Arg Arg Leu Gln Gln Glu Asp Gly	
	35 40 45
Ile Ser Phe Glu Tyr His Arg Tyr Pro Glu Leu Arg Glu Ala Leu Val	
	50 55 60
Ser Val Trp Leu Gln Cys Thr Ala Ile Ser Arg Ile Tyr Thr Val Gly	
65	70 75 80
Arg Ser Phe Glu Gly Arg Glu Leu Leu Val Ile Glu Leu Ser Asp Asn	
	85 90 95
Pro Gly Val His Glu Pro Gly Glu Pro Glu Phe Lys Tyr Ile Gly Asn	
	100 105 110
Met His Gly Asn Glu Ala Val Gly Arg Glu Leu Leu Ile Phe Leu Ala	
	115 120 125

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Gln Tyr Leu Cys Asn Glu Tyr Gln Lys Gly Asn Glu Thr Ile Val Asn
 130 135 140
 Leu Ile His Ser Thr Arg Ile His Ile Met Pro Ser Leu Asn Pro Asp
 145 150 155 160
 Gly Phe Glu Lys Ala Ala Ser Gln Pro Gly Glu Leu Lys Asp Trp Phe
 165 170 175
 Val Gly Arg Ser Asn Ala Gln Gly Ile Asp Leu Asn Arg Asn Phe Pro
 180 185 190
 Asp Leu Asp Arg Ile Val Tyr Val Asn Glu Lys Glu Gly Gly Pro Asn
 195 200 205
 Asn His Leu Leu Lys Asn Met Lys Lys Ile Val Asp Gln Asn Thr Lys
 210 215 220
 Leu Ala Pro Glu Thr Lys Ala Val Ile His Trp Ile Met Asp Ile Pro
 225 230 235 240
 Phe Val Leu Ser Ala Asn Leu His Gly Gly Asp Leu Val Ala Asn Tyr
 245 250 255
 Pro Tyr Asp Glu Thr Arg Ser Gly Ser Ala His Glu Tyr Ser Ser Ser
 260 265 270
 Pro Asp Asp Ala Ile Phe Gln Ser Leu Ala Arg Ala Tyr Ser Ser Phe
 275 280 285
 Asn Pro Ala Met Ser Asp Pro Asn Arg Pro Pro Cys Arg Lys Asn Asp
 290 295 300
 Asp Asp Ser Ser Phe Val Asp Gly Thr Thr Asn Gly Gly Ala Trp Tyr
 305 310 315 320
 Ser Val Pro Gly Gly Met Gln Asp Phe Asn Tyr Leu Ser Ser Asn Cys
 325 330 335
 Phe Glu Ile Thr Val Glu Leu Ser Cys Glu Lys Phe Pro Pro Glu Glu
 340 345 350
 Thr Leu Lys Thr Tyr Trp Glu Asp Asn Lys Asn Ser Leu Ile Ser Tyr
 355 360 365
 Leu Glu Gln Ile His Arg Gly Val Lys Gly Phe Val Arg Asp Leu Gln
 370 375 380
 Gly Asn Pro Ile Ala Asn Ala Thr Ile Ser Val Glu Gly Ile Asp His
 385 390 395 400
 Asp Val Thr Ser Ala Lys Asp Gly Asp Tyr Trp Arg Leu Leu Ile Pro
 405 410 415
 Gly Asn Tyr Lys Leu Thr Ala Ser Ala Pro Gly Tyr Leu Ala Ile Thr
 420 425 430
 Lys Lys Val Ala Val Pro Tyr Ser Pro Ala Ala Gly Val Asp Phe Glu
 435 440 445

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Leu Glu Ser Phe Ser Glu Arg Lys Glu Glu Glu Lys Glu Glu Leu Met
 450 455 460

Glu Trp Trp Lys Met Met Ser Glu Thr Leu Asn Phe
 465 470 475

<210> 68

<211> 355

<212> PRT

<213> Homo Sapiens

<400> 68

Met Asp Gln Phe Pro Glu Ser Val Thr Glu Asn Phe Glu Tyr Asp Asp
 1 5 10 15

Leu Ala Glu Ala Cys Tyr Ile Gly Asp Ile Val Val Phe Gly Thr Val
 20 25 30

Phe Leu Ser Ile Phe Tyr Ser Val Ile Phe Ala Ile Gly Leu Val Gly
 35 40 45

Asn Leu Leu Val Val Phe Ala Leu Thr Asn Ser Lys Lys Pro Lys Ser
 50 55 60

Val Thr Asp Ile Tyr Leu Leu Asn Leu Ala Leu Ser Asp Leu Leu Phe
 65 70 75 80

Val Ala Thr Leu Pro Phe Trp Thr His Tyr Leu Ile Asn Glu Lys Gly
 85 90 95

Leu His Asn Ala Met Cys Lys Phe Thr Thr Ala Phe Phe Phe Ile Gly
 100 105 110

Phe Phe Gly Ser Ile Phe Phe Ile Thr Val Ile Ser Ile Asp Arg Tyr
 115 120 125

Leu Ala Ile Val Leu Ala Ala Asn Ser Met Asn Asn Arg Thr Val Gln
 130 135 140

His Gly Val Thr Ile Ser Leu Gly Val Trp Ala Ala Ala Ile Leu Val
 145 150 155 160

Ala Ala Pro Gln Phe Met Phe Thr Lys Gln Lys Glu Asn Glu Cys Leu
 165 170 175

Gly Asp Tyr Pro Glu Val Leu Gln Glu Ile Trp Pro Val Leu Arg Asn
 180 185 190

Val Glu Thr Asn Phe Leu Gly Phe Leu Leu Pro Leu Leu Ile Met Ser
 195 200 205

Tyr Cys Tyr Phe Arg Ile Ile Gln Thr Leu Phe Ser Cys Lys Asn His
 210 215 220

Lys Lys Ala Lys Ala Ile Lys Leu Ile Leu Leu Val Val Ile Val Phe
 225 230 235 240

Phe Leu Phe Trp Thr Pro Tyr Asn Val Met Ile Phe Leu Glu Thr Leu
 245 250 255

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Lys Leu Tyr Asp Phe Phe Pro Ser Cys Asp Met Arg Lys Asp Leu Arg
 260 265 270
 Leu Ala Leu Ser Val Thr Glu Thr Val Ala Phe Ser His Cys Cys Leu
 275 280 285
 Asn Pro Leu Ile Tyr Ala Phe Ala Gly Glu Lys Phe Arg Arg Tyr Leu
 290 295 300
 Tyr His Leu Tyr Gly Lys Cys Leu Ala Val Leu Cys Gly Arg Ser Val
 305 310 315 320
 His Val Asp Phe Ser Ser Ser Glu Ser Gln Arg Ser Arg His Gly Ser
 325 330 335
 Val Leu Ser Ser Asn Phe Thr Tyr His Thr Ser Asp Gly Asp Ala Leu
 340 345 350
 Leu Leu Leu
 355

<210> 69
 <211> 767
 <212> PRT
 <213> Homo Sapiens

<400> 69

Met Ser Gln Arg Pro Arg Ala Pro Arg Ser Ala Leu Trp Leu Leu Ala
 1 5 10 15
 Pro Pro Leu Leu Arg Trp Ala Pro Pro Leu Leu Thr Val Leu His Ser
 20 25 30
 Asp Leu Phe Gln Ala Leu Leu Asp Ile Leu Asp Tyr Tyr Glu Ala Ser
 35 40 45
 Leu Ser Glu Ser Gln Lys Tyr Arg Tyr Gln Asp Glu Asp Thr Pro Pro
 50 55 60
 Leu Glu His Ser Pro Ala His Leu Pro Asn Gln Ala Asn Ser Pro Pro
 65 70 75 80
 Val Ile Val Asn Thr Asp Thr Leu Glu Ala Pro Gly Tyr Glu Leu Gln
 85 90 95
 Val Asn Gly Thr Glu Gly Glu Met Glu Tyr Glu Glu Ile Thr Leu Glu
 100 105 110
 Arg Gly Asn Ser Gly Leu Gly Phe Ser Ile Ala Gly Gly Thr Asp Asn
 115 120 125
 Pro His Ile Gly Asp Asp Pro Ser Ile Phe Ile Thr Lys Ile Ile Pro
 130 135 140
 Gly Gly Ala Ala Ala Gln Asp Gly Arg Leu Arg Val Asn Asp Ser Ile
 145 150 155 160
 Leu Phe Val Asn Glu Val Asp Val Arg Glu Val Thr His Ser Ala Ala

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165										170					175				
Val	Glu	Ala	Leu	Lys	Glu	Ala	Gly	Ser	Ile	Val	Arg	Leu	Tyr	Val	Met				
			180					185					190						
Arg	Arg	Lys	Pro	Pro	Ala	Glu	Lys	Val	Met	Glu	Ile	Lys	Leu	Ile	Lys				
		195					200					205							
Gly	Pro	Lys	Gly	Leu	Gly	Phe	Ser	Ile	Ala	Gly	Gly	Val	Gly	Asn	Gln				
	210					215					220								
His	Ile	Pro	Gly	Asp	Asn	Ser	Ile	Tyr	Val	Thr	Lys	Ile	Ile	Glu	Gly				
225					230					235					240				
Gly	Ala	Ala	His	Lys	Asp	Gly	Arg	Leu	Gln	Ile	Gly	Asp	Lys	Ile	Leu				
				245					250					255					
Ala	Val	Asn	Ser	Val	Gly	Leu	Glu	Asp	Val	Met	His	Glu	Asp	Ala	Val				
			260					265					270						
Ala	Ala	Leu	Lys	Asn	Thr	Tyr	Asp	Val	Val	Tyr	Leu	Lys	Val	Ala	Lys				
		275					280					285							
Pro	Ser	Asn	Ala	Tyr	Leu	Ser	Asp	Ser	Tyr	Ala	Pro	Pro	Asp	Ile	Thr				
	290					295					300								
Thr	Ser	Tyr	Ser	Gln	His	Leu	Asp	Asn	Glu	Ile	Ser	His	Ser	Ser	Tyr				
305				310						315					320				
Leu	Gly	Thr	Asp	Tyr	Pro	Thr	Ala	Met	Thr	Pro	Thr	Ser	Pro	Arg	Arg				
				325					330					335					
Tyr	Ser	Pro	Val	Ala	Lys	Asp	Leu	Leu	Gly	Glu	Glu	Asp	Ile	Pro	Arg				
			340					345					350						
Glu	Pro	Arg	Arg	Ile	Val	Ile	His	Arg	Gly	Ser	Thr	Gly	Leu	Gly	Phe				
		355					360					365							
Asn	Ile	Val	Gly	Gly	Glu	Asp	Gly	Glu	Gly	Ile	Phe	Ile	Ser	Phe	Ile				
	370					375					380								
Leu	Ala	Gly	Gly	Pro	Ala	Asp	Leu	Ser	Gly	Glu	Leu	Arg	Lys	Gly	Asp				
385					390					395					400				
Gln	Ile	Leu	Ser	Val	Asn	Gly	Val	Asp	Leu	Arg	Asn	Ala	Ser	His	Glu				
				405					410					415					
Gln	Ala	Ala	Ile	Ala	Leu	Lys	Asn	Ala	Gly	Gln	Thr	Val	Thr	Ile	Ile				
			420					425					430						
Ala	Gln	Tyr	Lys	Pro	Glu	Glu	Tyr	Ser	Arg	Phe	Glu	Ala	Lys	Ile	His				
		435					440					445							
Asp	Leu	Arg	Glu	Gln	Leu	Met	Asn	Ser	Ser	Leu	Gly	Ser	Gly	Thr	Ala				
	450					455					460								
Ser	Leu	Arg	Ser	Asn	Pro	Lys	Arg	Gly	Phe	Tyr	Ile	Arg	Ala	Leu	Phe				
465					470					475					480				
Asp	Tyr	Asp	Lys	Thr	Lys	Asp	Cys	Gly	Phe	Leu	Ser	Gln	Ala	Leu	Ser				

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485										490					495				
Phe	Arg	Phe	Gly	Asp	Val	Leu	His	Val	Ile	Asp	Ala	Ser	Asp	Glu	Glu				
			500					505					510						
Trp	Trp	Gln	Ala	Arg	Arg	Val	His	Ser	Asp	Ser	Glu	Thr	Asp	Asp	Ile				
		515					520					525							
Gly	Phe	Ile	Pro	Ser	Lys	Arg	Arg	Val	Glu	Arg	Arg	Glu	Trp	Ser	Arg				
	530					535					540								
Leu	Lys	Ala	Lys	Asp	Trp	Gly	Ser	Ser	Ser	Gly	Ser	Gln	Gly	Arg	Glu				
545					550					555					560				
Asp	Ser	Val	Leu	Ser	Tyr	Glu	Thr	Val	Thr	Gln	Met	Glu	Val	His	Tyr				
				565					570					575					
Ala	Arg	Pro	Ile	Ile	Ile	Leu	Gly	Pro	Thr	Lys	Asp	Arg	Ala	Asn	Asp				
			580					585					590						
Asp	Leu	Leu	Ser	Glu	Phe	Pro	Asp	Lys	Phe	Gly	Ser	Cys	Val	Pro	His				
		595					600					605							
Thr	Thr	Arg	Pro	Lys	Arg	Glu	Tyr	Glu	Ile	Asp	Gly	Arg	Asp	Tyr	His				
	610					615					620								
Phe	Val	Ser	Ser	Arg	Glu	Lys	Met	Glu	Lys	Asp	Ile	Gln	Ala	His	Lys				
625					630					635					640				
Phe	Ile	Glu	Ala	Gly	Gln	Tyr	Asn	Ser	His	Leu	Tyr	Gly	Thr	Ser	Val				
				645					650					655					
Gln	Ser	Val	Arg	Glu	Val	Ala	Glu	Gln	Gly	Lys	His	Cys	Ile	Leu	Asp				
			660					665					670						
Val	Ser	Ala	Asn	Ala	Val	Arg	Arg	Leu	Gln	Ala	Ala	His	Leu	His	Pro				
		675					680					685							
Ile	Ala	Ile	Phe	Ile	Arg	Pro	Arg	Ser	Leu	Glu	Asn	Val	Leu	Glu	Ile				
	690					695					700								
Asn	Lys	Arg	Ile	Thr	Glu	Glu	Gln	Ala	Arg	Lys	Ala	Phe	Asp	Arg	Ala				
705					710					715					720				
Thr	Lys	Leu	Glu	Gln	Glu	Phe	Thr	Glu	Cys	Phe	Ser	Ala	Ile	Val	Glu				
			725						730					735					
Gly	Asp	Ser	Phe	Glu	Glu	Ile	Tyr	His	Lys	Val	Lys	Arg	Val	Ile	Glu				
			740					745					750						
Asp	Leu	Ser	Gly	Pro	Tyr	Ile	Trp	Val	Pro	Ala	Arg	Glu	Arg	Leu					
		755					760					765							

<210> 70
 <211> 752
 <212> PRT
 <213> Homo Sapiens
 <400> 70

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Met Val Val Asp Glu Gln Gln Arg Leu Thr Ala Gln Leu Thr Leu Gln
 1 5 10 15
 Arg Gln Lys Ile Gln Glu Leu Thr Thr Asn Ala Lys Glu Thr His Thr
 20 25 30
 Lys Leu Ala Leu Ala Glu Ala Arg Val Gln Glu Glu Glu Gln Lys Ala
 35 40 45
 Thr Arg Leu Glu Lys Glu Leu Gln Thr Gln Thr Thr Lys Phe His Gln
 50 55 60
 Asp Gln Asp Thr Ile Met Ala Lys Leu Thr Asn Glu Asp Ser Gln Asn
 65 70 75 80
 Arg Gln Leu Gln Gln Lys Leu Ala Ala Leu Ser Arg Gln Ile Asp Glu
 85 90 95
 Leu Glu Glu Thr Asn Arg Ser Leu Arg Lys Ala Glu Glu Glu Leu Gln
 100 105 110
 Asp Ile Lys Glu Lys Ile Ser Lys Gly Glu Tyr Gly Asn Ala Gly Ile
 115 120 125
 Met Ala Glu Val Glu Glu Leu Ile Lys Met Glu Glu Gln Cys Arg Asp
 130 135 140
 Leu Asn Lys Arg Leu Glu Arg Glu Thr Leu Gln Ser Lys Asp Phe Lys
 145 150 155 160
 Leu Glu Val Glu Lys Leu Ser Lys Arg Ile Met Ala Leu Glu Lys Leu
 165 170 175
 Glu Asp Ala Phe Asn Lys Ser Lys Gln Glu Cys Tyr Ser Leu Lys Cys
 180 185 190
 Asn Leu Glu Lys Glu Arg Met Thr Thr Lys Gln Leu Ser Gln Glu Leu
 195 200 205
 Glu Ser Leu Lys Val Arg Ile Lys Glu Leu Glu Ala Ile Glu Ser Arg
 210 215 220
 Leu Glu Lys Thr Glu Phe Thr Leu Lys Glu Asp Leu Thr Lys Leu Lys
 225 230 235 240
 Thr Leu Thr Val Met Phe Val Asp Glu Arg Lys Thr Met Ser Glu Lys
 245 250 255
 Leu Lys Lys Thr Glu Asp Lys Leu Gln Ala Ala Ser Ser Gln Leu Gln
 260 265 270
 Val Glu Gln Asn Lys Val Thr Thr Val Thr Glu Lys Leu Ile Glu Glu
 275 280 285
 Thr Lys Arg Ala Leu Lys Ser Lys Thr Asp Val Glu Glu Lys Met Tyr
 290 295 300
 Ser Val Thr Lys Glu Arg Asp Asp Leu Lys Asn Lys Leu Lys Ala Glu
 305 310 315 320

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Glu Glu Lys Gly Asn Asp Leu Leu Ser Arg Val Asn Met Leu Lys Asn
 325 330 335
 Arg Leu Gln Ser Leu Glu Ala Ile Glu Lys Asp Phe Leu Lys Asn Lys
 340 345 350
 Leu Asn Gln Asp Ser Gly Lys Ser Thr Thr Ala Leu His Gln Glu Asn
 355 360 365
 Asn Lys Ile Lys Glu Leu Ser Gln Glu Val Glu Arg Leu Lys Leu Lys
 370 375 380
 Leu Lys Asp Met Lys Ala Ile Glu Asp Asp Leu Met Lys Thr Glu Asp
 385 390 395 400
 Glu Tyr Glu Thr Leu Glu Arg Arg Tyr Ala Asn Glu Arg Asp Lys Ala
 405 410 415
 Gln Phe Leu Ser Lys Glu Leu Glu His Val Lys Met Glu Leu Ala Lys
 420 425 430
 Tyr Lys Leu Ala Glu Lys Thr Glu Thr Ser His Glu Gln Trp Leu Phe
 435 440 445
 Lys Arg Leu Gln Glu Glu Glu Ala Lys Ser Gly His Leu Ser Arg Glu
 450 455 460
 Val Asp Ala Leu Lys Glu Lys Ile His Glu Tyr Met Ala Thr Glu Asp
 465 470 475 480
 Leu Ile Cys His Leu Gln Gly Asp His Ser Val Cys Lys Lys Lys Leu
 485 490 495
 Asn Gln Gln Glu Asn Arg Asn Arg Asp Leu Gly Arg Glu Ile Glu Asn
 500 505 510
 Leu Thr Lys Glu Leu Glu Arg Tyr Arg His Phe Ser Lys Ser Leu Arg
 515 520 525
 Pro Ser Leu Asn Gly Arg Arg Ile Ser Asp Pro Gln Val Phe Ser Lys
 530 535 540
 Glu Val Gln Thr Glu Ala Val Asp Asn Glu Pro Pro Asp Tyr Lys Ser
 545 550 555 560
 Leu Ile Pro Leu Glu Arg Ala Val Ile Asn Gly Gln Leu Tyr Glu Glu
 565 570 575
 Ser Glu Asn Gln Asp Glu Asp Pro Asn Asp Glu Gly Ser Val Leu Ser
 580 585 590
 Phe Lys Cys Ser Gln Ser Thr Pro Cys Pro Val Asn Arg Lys Leu Trp
 595 600 605
 Ile Pro Trp Met Lys Ser Lys Glu Gly His Leu Gln Asn Gly Lys Met
 610 615 620
 Gln Thr Lys Pro Asn Ala Asn Phe Val Gln Pro Gly Asp Leu Val Leu
 625 630 635 640

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Ser His Thr Pro Gly Gln Pro Leu His Ile Lys Val Thr Pro Asp His
645 650 655

Val Gln Asn Thr Ala Thr Leu Glu Ile Thr Ser Pro Thr Thr Glu Ser
660 665 670

Pro His Ser Tyr Thr Ser Thr Ala Val Ile Pro Asn Cys Gly Thr Pro
675 680 685

Lys Gln Arg Ile Thr Ile Leu Gln Asn Ala Ser Ile Thr Pro Val Lys
690 695 700

Ser Lys Thr Ser Thr Glu Asp Leu Met Asn Leu Glu Gln Gly Met Ser
705 710 715 720

Pro Ile Thr Met Ala Thr Phe Ala Arg Ala Gln Thr Pro Glu Ser Cys
725 730 735

Gly Ser Leu Thr Pro Glu Arg Thr Met Ser Leu Phe Arg Phe Trp Leu
740 745 750

<210> 71
<211> 105
<212> PRT
<213> Homo Sapiens

<400> 71

Met Gln Thr Gln Ala Glu Ala Leu Thr Ala Gly Met Ala Gly Val Ala
1 5 10 15

Thr Ala Ala Ala Gly Ala Trp Thr Gln Pro Gln Leu Arg Pro Val Glu
20 25 30

Leu Pro Gln Arg Thr Arg Gln Val Arg Ala Glu Thr Pro Arg Leu Pro
35 40 45

Gln Gly Val Thr Asn Ala Ala Ala His Ile His Pro Gln Arg Ala Phe
50 55 60

Pro Asp Pro Leu Gly Gly Gly Asn Arg Pro Trp Val Pro Gly Thr Arg
65 70 75 80

Cys Arg Ala Pro Pro Lys Gly Gly Trp Glu Gly Ser His Ser Glu Trp
85 90 95

Gln Asp Pro Gly Arg Pro Leu Glu Ser
100 105

<210> 72
<211> 225
<212> PRT
<213> Homo Sapiens

<400> 72

Met Asn Ser Asn Val Glu Asn Leu Pro Pro His Ile Ile Arg Leu Val
1 5 10 15

Tyr Lys Glu Val Thr Thr Leu Thr Ala Asp Pro Pro Asp Gly Ile Lys

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20							25					30			
Val	Phe	Pro	Asn	Glu	Glu	Asp	Leu	Thr	Asp	Leu	Gln	Val	Thr	Ile	Glu
35			40				45								
Gly	Pro	Glu	Gly	Thr	Pro	Tyr	Ala	Gly	Gly	Leu	Phe	Arg	Met	Lys	Leu
50			55				60								
Leu	Leu	Gly	Lys	Asp	Phe	Pro	Ala	Ser	Pro	Pro	Lys	Gly	Tyr	Phe	Leu
65					70	75				80					
Thr	Lys	Ile	Phe	His	Pro	Asn	Val	Gly	Ala	Asn	Gly	Glu	Ile	Cys	Val
				85	90				95						
Asn	Val	Leu	Lys	Arg	Asp	Trp	Thr	Ala	Glu	Leu	Gly	Ile	Arg	His	Val
100			105				110								
Leu	Leu	Thr	Ile	Lys	Cys	Leu	Leu	Ile	His	Pro	Asn	Pro	Glu	Ser	Ala
115			120				125								
Leu	Asn	Glu	Glu	Ala	Gly	Arg	Leu	Leu	Leu	Glu	Asn	Tyr	Glu	Glu	Tyr
130			135				140								
Ala	Ala	Arg	Ala	Arg	Leu	Leu	Thr	Glu	Ile	His	Gly	Gly	Ala	Gly	Gly
145			150				155				160				
Pro	Ser	Gly	Arg	Ala	Glu	Ala	Gly	Arg	Ala	Leu	Ala	Ser	Gly	Thr	Glu
				165	170				175						
Ala	Ser	Ser	Thr	Asp	Pro	Gly	Ala	Pro	Gly	Gly	Pro	Gly	Gly	Ala	Glu
180			185				190								
Gly	Pro	Met	Ala	Lys	Lys	His	Ala	Gly	Glu	Arg	Asp	Lys	Lys	Leu	Ala
195			200				205								
Ala	Lys	Lys	Lys	Thr	Asp	Lys	Lys	Arg	Ala	Leu	Arg	Ala	Leu	Arg	Arg
210			215				220								

Leu
225

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<210> 73
<211> 208
<212> PRT
<213> Homo Sapiens
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<400> 73

Pro	His	Pro	Met	Pro	Leu	Arg	Leu	Pro	Thr	Pro	Gly	Gly	Asn	Gly	Gln
1				5					10					15	
Ala	Gly	Arg	Pro	Cys	Arg	Ser	Thr	Gly	Gln	Gly	Asn	Lys	Arg	Gly	Ala
			20					25					30		
Ala	Lys	Cys	Pro	Asp	Gln	Glu	Ala	Pro	Tyr	Phe	Arg	Gly	Lys	Gly	His
		35					40					45			
Val	Val	Leu	Ala	Pro	His	Pro	Ile	Pro	Ser	His	Leu	Gly	Ala	Pro	Pro
	50					55					60				

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Pro His Ser Leu His Leu Gln Gly Asn Leu Val Leu His Ala Gly Ala
65 70 75 80

Leu Ile Phe Leu Gly Gly Gly Arg Arg Glu Gly Trp Pro Leu Gly Glu
85 90 95

Pro Pro Thr Trp Gly Ser Ser Lys Asp Gly Ala Asp Thr Ser Trp Ala
100 105 110

Val Pro Ala Pro Pro Ala His Gln Asp Pro Pro Leu Ala Ala Ile Gln
115 120 125

Leu Val Pro Lys His Leu Lys Pro Gln Ser Trp Ile Arg Ser Ser Ile
130 135 140

Pro Pro Leu Leu Gly Pro Leu Gly Arg Leu Leu Pro Thr Asp Arg Cys
145 150 155 160

Ser Pro His Leu Gly Arg Phe Trp Val Gly Lys Pro Pro His Thr Gly
165 170 175

Asn Ser His Leu Ala Pro Cys Arg Ile His Pro Arg Ile Arg Pro Phe
180 185 190

Ile His Arg Ser Val His Pro Cys Pro Gln Leu Thr Ala Arg His His
195 200 205

<210> 74

<211> 109

<212> PRT

<213> Homo Sapiens

<400> 74

Met Ala Tyr Gln Leu Tyr Arg Asn Thr Thr Leu Gly Asn Ser Leu Gln
1 5 10 15

Glu Ser Leu Asp Glu Leu Ile Gln Ser Gln Gln Ile Thr Pro Gln Leu
20 25 30

Ala Leu Gln Val Leu Leu Gln Phe Asp Lys Ala Ile Asn Ala Ala Leu
35 40 45

Ala Gln Arg Val Arg Asn Arg Val Asn Phe Arg Gly Ser Leu Asn Thr
50 55 60

Tyr Arg Phe Cys Asp Asn Val Trp Thr Phe Val Leu Asn Asp Val Glu
65 70 75 80

Phe Arg Glu Val Thr Glu Leu Ile Lys Val Asp Lys Val Lys Ile Val
85 90 95

Ala Cys Asp Gly Lys Asn Thr Gly Ser Asn Thr Thr Glu
100 105

<210> 75

<211> 693

<212> PRT

<213> Homo Sapiens

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<400> 75

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Met Ala Leu Cys Asn Gly Asp Ser Lys Leu Glu Asn Ala Gly Gly Asp
1           5           10           15
Leu Lys Asp Gly His His His Tyr Glu Gly Ala Val Val Ile Leu Asp
20           25           30
Ala Gly Ala Gln Tyr Gly Lys Val Ile Asp Arg Arg Val Arg Glu Leu
35           40           45
Phe Val Gln Ser Glu Ile Phe Pro Leu Glu Thr Pro Ala Phe Ala Ile
50           55           60
Lys Glu Gln Gly Phe Arg Ala Ile Ile Ile Ser Gly Gly Pro Asn Ser
65           70           75           80
Val Tyr Ala Glu Asp Ala Pro Trp Phe Asp Pro Ala Ile Phe Thr Ile
85           90           95
Gly Lys Pro Val Leu Gly Ile Cys Tyr Gly Met Gln Met Met Asn Lys
100          105          110
Val Phe Gly Gly Thr Val His Lys Lys Ser Val Arg Glu Asp Gly Val
115          120          125
Phe Asn Ile Ser Val Asp Asn Thr Cys Ser Leu Phe Arg Gly Leu Gln
130          135          140
Lys Glu Glu Val Val Leu Leu Thr His Gly Asp Ser Val Asp Lys Val
145          150          155          160
Ala Asp Gly Phe Lys Val Val Ala Arg Ser Gly Asn Ile Val Ala Gly
165          170          175
Ile Ala Asn Glu Ser Lys Lys Leu Tyr Gly Ala Gln Phe His Pro Glu
180          185          190
Val Gly Leu Thr Glu Asn Gly Lys Val Ile Leu Lys Asn Phe Leu Tyr
195          200          205
Asp Ile Ala Gly Cys Ser Gly Thr Phe Thr Val Gln Asn Arg Glu Leu
210          215          220
Glu Cys Ile Arg Glu Ile Lys Glu Arg Val Gly Thr Ser Lys Val Leu
225          230          235          240
Val Leu Leu Ser Gly Gly Val Asp Ser Thr Val Cys Thr Ala Leu Leu
245          250          255
Asn Arg Ala Leu Asn Gln Glu Gln Val Ile Ala Val His Ile Asp Asn
260          265          270
Gly Phe Met Arg Lys Arg Glu Ser Gln Ser Val Glu Glu Ala Leu Lys
275          280          285
Lys Leu Gly Ile Gln Val Lys Val Ile Asn Ala Ala His Ser Phe Tyr
290          295          300
Asn Gly Thr Thr Thr Leu Pro Ile Ser Asp Glu Asp Arg Thr Pro Arg

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305		310		315		320
Lys Arg Ile Ser	Lys Thr Leu Asn Met Thr Thr Ser Pro Glu Glu Lys					
	325			330		335
Arg Lys Ile Ile Gly Asp Thr Phe Val Lys Ile Ala Asn Glu Val Ile						
	340		345			350
Gly Glu Met Asn Leu Lys Pro Glu Glu Val Phe Leu Ala Gln Gly Thr						
	355		360			365
Leu Arg Pro Asp Leu Ile Glu Ser Ala Ser Leu Val Ala Ser Gly Lys						
	370		375			380
Ala Glu Leu Ile Lys Thr His His Asn Asp Thr Glu Leu Ile Arg Lys						
	385		390			395
Leu Arg Glu Glu Gly Lys Val Ile Glu Pro Leu Lys Asp Phe His Lys						
		405		410		415
Asp Glu Val Arg Ile Leu Gly Arg Glu Leu Gly Leu Pro Glu Glu Leu						
		420		425		430
Val Ser Arg His Pro Phe Pro Gly Pro Gly Leu Ala Ile Arg Val Ile						
		435		440		445
Cys Ala Glu Glu Pro Tyr Ile Cys Lys Asp Phe Pro Glu Thr Asn Asn						
	450		455			460
Ile Leu Lys Ile Val Ala Asp Phe Ser Ala Ser Val Lys Lys Pro His						
	465		470			475
Thr Leu Leu Gln Arg Val Lys Ala Cys Thr Thr Glu Glu Asp Gln Glu						
		485		490		495
Lys Leu Met Gln Ile Thr Ser Leu His Ser Leu Asn Ala Phe Leu Leu						
	500		505			510
Pro Ile Lys Thr Val Gly Val Gln Gly Asp Cys Arg Ser Tyr Ser Tyr						
	515		520			525
Val Cys Gly Ile Ser Ser Lys Asp Glu Pro Asp Trp Glu Ser Leu Ile						
	530		535			540
Phe Leu Ala Arg Leu Ile Pro Arg Met Cys His Asn Val Asn Arg Val						
	545		550			555
Val Tyr Ile Phe Gly Pro Pro Val Lys Glu Pro Pro Thr Asp Val Thr						
		565		570		575
Pro Thr Phe Leu Thr Thr Gly Val Leu Ser Thr Leu Arg Gln Ala Asp						
	580		585			590
Phe Glu Ala His Asn Ile Leu Arg Glu Ser Gly Tyr Ala Gly Lys Ile						
	595		600			605
Ser Gln Met Pro Val Ile Leu Thr Pro Leu His Phe Asp Arg Asp Pro						
	610		615			620
Leu Gln Lys Gln Pro Ser Cys Gln Arg Ser Val Val Ile Arg Thr Phe						

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625						630						635						640
Ile	Thr	Ser	Asp	Phe	Met	Thr	Gly	Ile	Pro	Ala	Thr	Pro	Gly	Asn	Glu			
				645					650					655				
Ile	Pro	Val	Glu	Val	Val	Leu	Lys	Met	Val	Thr	Glu	Ile	Lys	Lys	Ile			
				660					665					670				
Pro	Gly	Ile	Ser	Arg	Ile	Met	Tyr	Asp	Leu	Thr	Ser	Lys	Pro	Pro	Gly			
				675					680					685				
Thr	Thr	Glu	Trp	Glu														
					690													

<210>	76
<211>	143
<212>	PRT
<213>	Homo Sapiens

<400> 76

Met	Ser	Gly	Arg	Gly	Lys	Thr	Gly	Gly	Lys	Ala	Arg	Ala	Lys	Ala	Lys
1				5					10					15	
Ser	Arg	Ser	Ser	Arg	Ala	Gly	Leu	Gln	Phe	Pro	Val	Gly	Arg	Val	His
			20					25					30		
Arg	Leu	Leu	Arg	Lys	Gly	His	Tyr	Ala	Glu	Arg	Val	Gly	Ala	Gly	Ala
		35					40					45			
Pro	Val	Tyr	Leu	Ala	Ala	Val	Leu	Glu	Tyr	Leu	Thr	Ala	Glu	Ile	Leu
	50					55					60				
Glu	Leu	Ala	Gly	Asn	Ala	Ala	Arg	Asp	Asn	Lys	Lys	Thr	Arg	Ile	Ile
65					70					75					80
Pro	Arg	His	Leu	Gln	Leu	Ala	Ile	Arg	Asn	Asp	Glu	Glu	Leu	Asn	Lys
				85					90					95	
Leu	Leu	Gly	Gly	Val	Thr	Ile	Ala	Gln	Gly	Gly	Val	Leu	Pro	Asn	Ile
			100					105					110		
Gln	Ala	Val	Leu	Leu	Pro	Lys	Lys	Thr	Ser	Ala	Thr	Val	Gly	Pro	Lys
		115					120					125			
Ala	Pro	Ser	Gly	Gly	Lys	Lys	Ala	Thr	Gln	Ala	Ser	Gln	Glu	Tyr	
	130					135					140				

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<210> 77
<211> 126
<212> PRT
<213> Homo Sapiens
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<400> 77

Met	Pro	Glu	Pro	Ala	Lys	Ser	Ala	Pro	Ala	Pro	Lys	Lys	Gly	Ser	Lys
1				5					10					15	
Lys	Ala	Val	Thr	Lys	Ala	Gln	Lys	Lys	Asp	Gly	Lys	Lys	Arg	Lys	Arg
			20					25					30		

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Ser Arg Lys Glu Ser Tyr Ser Val Tyr Val Tyr Lys Val Leu Lys Gln
 35 40 45
 Val His Pro Asp Thr Gly Ile Ser Ser Lys Ala Met Gly Ile Met Asn
 50 55 60
 Ser Phe Val Asn Asp Ile Phe Glu Arg Ile Ala Gly Glu Ala Ser Arg
 65 70 75 80
 Leu Ala His Tyr Asn Lys Arg Ser Thr Ile Thr Ser Arg Glu Ile Gln
 85 90 95
 Thr Ala Val Arg Leu Leu Leu Pro Gly Glu Leu Ala Lys His Ala Val
 100 105 110
 Ser Glu Gly Thr Lys Ala Val Thr Lys Tyr Thr Ser Ser Lys
 115 120 125
 <210> 78
 <211> 664
 <212> PRT
 <213> Homo Sapiens
 <400> 78
 Met Lys Thr Gly Pro Phe Phe Leu Cys Leu Leu Gly Thr Ala Ala Ala
 1 5 10 15
 Ile Pro Thr Asn Ala Arg Leu Leu Ser Asp His Ser Lys Pro Thr Ala
 20 25 30
 Glu Thr Val Ala Pro Asp Asn Thr Ala Ile Pro Ser Leu Trp Ala Glu
 35 40 45
 Ala Glu Glu Asn Glu Lys Glu Thr Ala Val Ser Thr Glu Asp Asp Ser
 50 55 60
 His His Lys Ala Glu Lys Ser Ser Val Leu Lys Ser Lys Glu Glu Ser
 65 70 75 80
 His Glu Gln Ser Ala Glu Gln Gly Lys Ser Ser Ser Gln Glu Leu Gly
 85 90 95
 Leu Lys Asp Gln Glu Asp Ser Asp Gly His Leu Ser Val Asn Leu Glu
 100 105 110
 Tyr Ala Pro Thr Glu Gly Thr Leu Asp Ile Lys Glu Asp Met Ile Glu
 115 120 125
 Pro Gln Glu Lys Lys Leu Ser Glu Asn Thr Asp Phe Leu Ala Pro Gly
 130 135 140
 Val Ser Ser Phe Thr Asp Ser Asn Gln Gln Glu Ser Ile Thr Lys Arg
 145 150 155 160
 Glu Glu Asn Gln Glu Gln Pro Arg Asn Tyr Ser His His Gln Leu Asn
 165 170 175
 Arg Ser Ser Lys His Ser Gln Gly Leu Arg Asp Gln Gly Asn Gln Glu

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180					185					190					
Gln	Asp	Pro	Asn	Ile	Ser	Asn	Gly	Glu	Glu	Glu	Glu	Glu	Lys	Glu	Pro
		195					200					205			
Gly	Glu	Val	Gly	Thr	His	Asn	Asp	Asn	Gln	Glu	Arg	Lys	Thr	Glu	Leu
		210					215					220			
Pro	Arg	Glu	His	Ala	Asn	Ser	Lys	Gln	Glu	Glu	Asp	Asn	Thr	Gln	Ser
		225					230					235			
Asp	Asp	Ile	Leu	Glu	Glu	Ser	Asp	Gln	Pro	Thr	Gln	Val	Ser	Lys	Met
				245					250					255	
Gln	Glu	Asp	Glu	Phe	Asp	Gln	Gly	Asn	Gln	Glu	Gln	Glu	Asp	Asn	Ser
				260					265					270	
Asn	Ala	Glu	Met	Glu	Glu	Glu	Asn	Ala	Ser	Asn	Val	Asn	Lys	His	Ile
				275					280					285	
Gln	Glu	Thr	Glu	Trp	Gln	Ser	Gln	Glu	Gly	Lys	Thr	Gly	Leu	Glu	Ala
				290					295					300	
Ile	Ser	Asn	His	Lys	Glu	Thr	Glu	Glu	Lys	Thr	Val	Ser	Glu	Ala	Leu
				305					310					315	
Leu	Met	Glu	Pro	Thr	Asp	Asp	Gly	Asn	Thr	Thr	Pro	Arg	Asn	His	Gly
				325					330					335	
Val	Asp	Asp	Asp	Gly	Asp	Asp	Asp	Gly	Asp	Asp	Gly	Gly	Thr	Asp	Gly
				340					345					350	
Pro	Arg	His	Ser	Ala	Ser	Asp	Asp	Tyr	Phe	Ile	Pro	Ser	Gln	Ala	Phe
				355					360					365	
Leu	Glu	Ala	Glu	Arg	Ala	Gln	Ser	Ile	Ala	Tyr	His	Leu	Lys	Ile	Glu
				370					375					380	
Glu	Gln	Arg	Glu	Lys	Val	His	Glu	Asn	Glu	Asn	Ile	Gly	Thr	Thr	Glu
				385					390					395	
Pro	Gly	Glu	His	Gln	Glu	Ala	Lys	Lys	Ala	Glu	Asn	Ser	Ser	Asn	Glu
				405					410					415	
Glu	Glu	Thr	Ser	Ser	Glu	Gly	Asn	Met	Arg	Val	His	Ala	Val	Asp	Ser
				420					425					430	
Cys	Met	Ser	Phe	Gln	Cys	Lys	Arg	Gly	His	Ile	Cys	Lys	Ala	Asp	Gln
				435					440					445	
Gln	Gly	Lys	Pro	His	Cys	Val	Cys	Gln	Asp	Pro	Val	Thr	Cys	Pro	Pro
				450					455					460	
Thr	Lys	Pro	Leu	Asp	Gln	Val	Cys	Gly	Thr	Asp	Asn	Gln	Thr	Tyr	Ala
				465					470					475	
Ser	Ser	Cys	His	Leu	Phe	Ala	Thr	Lys	Cys	Arg	Leu	Glu	Gly	Thr	Lys
				485					490					495	
Lys	Gly	His	Gln	Leu	Gln	Leu	Asp	Tyr	Phe	Gly	Ala	Cys	Lys	Ser	Ile

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500					505					510					
Pro	Thr	Cys	Thr	Asp	Phe	Glu	Val	Ile	Gln	Phe	Pro	Leu	Arg	Met	Arg
		515					520					525			
Asp	Trp	Leu	Lys	Asn	Ile	Leu	Met	Gln	Leu	Tyr	Glu	Ala	Asn	Ser	Glu
	530					535					540				
His	Ala	Gly	Tyr	Leu	Asn	Glu	Lys	Gln	Arg	Asn	Lys	Val	Lys	Lys	Ile
545					550					555					560
Tyr	Leu	Asp	Glu	Lys	Arg	Leu	Leu	Ala	Gly	Asp	His	Pro	Ile	Asp	Leu
				565					570					575	
Leu	Leu	Arg	Asp	Phe	Lys	Lys	Asn	Tyr	His	Met	Tyr	Val	Tyr	Pro	Val
			580					585					590		
His	Trp	Gln	Phe	Ser	Glu	Leu	Asp	Gln	His	Pro	Met	Asp	Arg	Val	Leu
		595					600					605			
Thr	His	Ser	Glu	Leu	Ala	Pro	Leu	Arg	Ala	Ser	Leu	Val	Pro	Met	Glu
	610					615					620				
His	Cys	Ile	Thr	Arg	Phe	Phe	Glu	Glu	Cys	Asp	Pro	Asn	Lys	Asp	Lys
625					630					635					640
His	Ile	Thr	Leu	Lys	Glu	Trp	Gly	His	Cys	Phe	Gly	Ile	Lys	Glu	Glu
				645					650					655	
Asp	Ile	Asp	Glu	Asn	Leu	Leu	Phe								
			660												
<210> 79															
<211> 460															
<212> PRT															
<213> Homo Sapiens															
<400> 79															
Ala	Lys	Leu	Ala	Thr	Lys	Ser	Pro	Thr	Ile	Thr	Met	Met	Leu	Ser	Thr
1				5					10					15	
Glu	Gly	Arg	Glu	Gly	Phe	Val	Val	Lys	Val	Arg	Gly	Leu	Pro	Trp	Ser
			20					25					30		
Cys	Ser	Ala	Asp	Glu	Val	Met	Arg	Phe	Phe	Ser	Asp	Cys	Lys	Ile	Gln
		35					40					45			
Asn	Gly	Thr	Ser	Gly	Ile	Arg	Phe	Ile	Tyr	Thr	Arg	Glu	Gly	Arg	Pro
	50					55					60				
Ser	Gly	Glu	Ala	Phe	Val	Glu	Leu	Glu	Ser	Glu	Glu	Glu	Val	Lys	Leu
65					70					75					80
Ala	Leu	Lys	Lys	Asp	Arg	Glu	Thr	Met	Gly	His	Arg	Tyr	Val	Glu	Val
				85					90					95	
Phe	Lys	Ser	Asn	Ser	Val	Glu	Met	Asp	Trp	Val	Leu	Lys	His	Thr	Gly
			100					105					110		

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Pro Asn Ser Pro Asp Thr Ala Asn Asp Gly Phe Val Arg Leu Arg Gly
 115 120 125
 Leu Pro Phe Gly Cys Ser Lys Glu Glu Ile Val Gln Phe Phe Ser Gly
 130 135 140
 Leu Glu Ile Val Pro Asn Gly Met Thr Leu Pro Val Asp Phe Gln Gly
 145 150 155 160
 Arg Ser Thr Gly Glu Ala Phe Val Gln Phe Ala Ser Gln Glu Ile Ala
 165 170 175
 Glu Lys Ala Leu Lys Lys His Lys Glu Arg Ile Gly His Arg Tyr Ile
 180 185 190
 Glu Ile Phe Lys Ser Ser Arg Ala Glu Val Arg Thr His Tyr Asp Pro
 195 200 205
 Pro Arg Lys Leu Met Ala Met Gln Arg Pro Gly Pro Tyr Asp Arg Pro
 210 215 220
 Gly Ala Gly Arg Gly Tyr Asn Ser Ile Gly Arg Gly Ala Gly Phe Glu
 225 230 235 240
 Arg Met Arg Arg Gly Ala Tyr Gly Gly Gly Tyr Gly Gly Tyr Asp Asp
 245 250 255
 Tyr Gly Gly Tyr Asn Asp Gly Tyr Gly Phe Gly Ser Asp Arg Phe Gly
 260 265 270
 Arg Asp Leu Asn Tyr Cys Phe Ser Gly Met Ser Asp His Arg Tyr Gly
 275 280 285
 Asp Gly Gly Ser Ser Phe Gln Ser Thr Thr Gly His Cys Val His Met
 290 295 300
 Arg Gly Leu Pro Tyr Arg Ala Thr Glu Asn Asp Ile Tyr Asn Phe Phe
 305 310 315 320
 Ser Pro Leu Asn Pro Met Arg Val His Ile Glu Ile Gly Pro Asp Gly
 325 330 335
 Arg Val Thr Gly Glu Ala Asp Val Glu Phe Ala Thr His Glu Asp Ala
 340 345 350
 Val Ala Ala Met Ala Lys Asp Lys Ala Asn Met Gln His Arg Tyr Val
 355 360 365
 Glu Leu Phe Leu Asn Ser Thr Ala Gly Thr Ser Gly Gly Ala Tyr Asp
 370 375 380
 His Ser Tyr Val Glu Leu Phe Leu Asn Ser Thr Ala Gly Ala Ser Gly
 385 390 395 400
 Gly Ala Tyr Gly Ser Gln Met Met Gly Gly Met Gly Leu Ser Asn Gln
 405 410 415
 Ser Ser Tyr Gly Gly Pro Ala Ser Gln Gln Leu Ser Gly Gly Tyr Gly
 420 425 430

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Gly Gly Tyr Gly Gly Gln Ser Ser Met Ser Gly Tyr Asp Gln Val Leu
 435 440 445

Gln Glu Asn Ser Ser Asp Tyr Gln Ser Asn Leu Ala
 450 455 460

<210> 80

<211> 432

<212> PRT

<213> Homo Sapiens

<400> 80

Met Asp Glu Ala Val Gly Asp Leu Lys Gln Ala Leu Pro Cys Val Ala
 1 5 10 15

Glu Ser Pro Thr Val His Val Glu Val His Gln Arg Gly Ser Ser Thr
 20 25 30

Ala Lys Lys Glu Asp Ile Asn Leu Ser Val Arg Lys Leu Leu Asn Arg
 35 40 45

His Asn Ile Val Phe Gly Asp Tyr Thr Trp Thr Glu Phe Asp Glu Pro
 50 55 60

Phe Leu Thr Arg Asn Val Gln Ser Val Ser Ile Ile Asp Thr Glu Leu
 65 70 75 80

Lys Val Lys Asp Ser Gln Pro Ile Asp Leu Ser Ala Cys Thr Val Ala
 85 90 95

Leu His Ile Phe Gln Leu Asn Glu Asp Gly Pro Ser Ser Glu Asn Leu
 100 105 110

Glu Glu Glu Thr Glu Asn Ile Ile Ala Ala Asn His Trp Val Leu Pro
 115 120 125

Ala Ala Glu Phe His Gly Leu Trp Asp Ser Leu Val Tyr Asp Val Glu
 130 135 140

Val Lys Ser His Leu Leu Asp Tyr Val Met Thr Thr Leu Leu Phe Ser
 145 150 155 160

Asp Lys Asn Val Asn Ser Asn Leu Ile Thr Trp Asn Arg Val Val Leu
 165 170 175

Leu His Gly Pro Pro Gly Thr Gly Lys Thr Ser Leu Cys Lys Ala Leu
 180 185 190

Ala Gln Lys Leu Thr Ile Arg Leu Ser Ser Arg Tyr Arg Tyr Gly Gln
 195 200 205

Leu Ile Glu Ile Asn Ser His Ser Leu Phe Ser Lys Trp Phe Ser Glu
 210 215 220

Ser Gly Lys Leu Val Thr Lys Met Phe Gln Lys Ile Gln Asp Leu Ile
 225 230 235 240

Asp Asp Lys Asp Ala Leu Val Phe Val Leu Ile Asp Glu Val Glu Ser
 245 250 255

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Leu Thr Ala Ala Arg Asn Ala Cys Arg Ala Gly Thr Glu Pro Ser Asp
260 265 270

Ala Ile Arg Val Val Asn Ala Val Leu Thr Gln Ile Asp Gln Ile Lys
275 280 285

Arg His Ser Asn Val Val Ile Leu Thr Thr Ser Asn Ile Thr Glu Lys
290 295 300

Ile Asp Val Ala Phe Val Asp Arg Ala Asp Ile Lys Gln Tyr Ile Gly
305 310 315 320

Pro Pro Ser Ala Ala Ala Ile Phe Lys Ile Tyr Leu Ser Cys Leu Glu
325 330 335

Glu Leu Met Lys Cys Gln Ile Ile Tyr Pro Arg Gln Gln Leu Leu Thr
340 345 350

Leu Arg Glu Leu Glu Met Ile Gly Phe Ile Glu Asn Asn Val Ser Lys
355 360 365

Leu Ser Leu Leu Leu Asn Asp Ile Ser Arg Lys Ser Glu Gly Leu Ser
370 375 380

Gly Arg Val Leu Arg Lys Leu Pro Phe Leu Ala His Ala Leu Tyr Val
385 390 395 400

Gln Ala Pro Thr Val Thr Ile Glu Gly Phe Leu Gln Ala Leu Ser Leu
405 410 415

Ala Val Asp Lys Gln Phe Glu Glu Arg Lys Lys Leu Ala Ala Tyr Ile
420 425 430

<210> 81
<211> 653
<212> PRT
<213> Homo Sapiens

<400> 81

Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu Ala Ser
1 5 10 15

Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val
20 25 30

Gln Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg
35 40 45

Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr
50 55 60

Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala Tyr Val Gly Ala Val
65 70 75 80

Pro His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu Glu Leu
85 90 95

Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr

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100					105					110					
His	Leu	Asp	Gly	Tyr	Leu	Asp	Leu	Leu	Arg	Glu	Asn	Gln	Leu	Leu	Pro
	115						120					125			
Gly	Phe	Glu	Leu	Met	Gly	Ser	Ala	Ser	Gly	His	Phe	Thr	Asp	Phe	Glu
	130					135					140				
Asp	Lys	Gln	Gln	Val	Phe	Glu	Trp	Lys	Asp	Leu	Val	Ser	Ser	Leu	Ala
145						150					155				160
Arg	Arg	Tyr	Ile	Gly	Arg	Tyr	Gly	Leu	Ala	His	Val	Ser	Lys	Trp	Asn
				165					170					175	
Phe	Glu	Thr	Trp	Asn	Glu	Pro	Asp	His	His	Asp	Phe	Asp	Asn	Val	Ser
			180					185					190		
Met	Thr	Met	Gln	Gly	Phe	Leu	Asn	Tyr	Tyr	Asp	Ala	Cys	Ser	Glu	Gly
		195					200					205			
Leu	Arg	Ala	Ala	Ser	Pro	Ala	Leu	Arg	Leu	Gly	Gly	Pro	Gly	Asp	Ser
	210					215					220				
Phe	His	Thr	Pro	Pro	Arg	Ser	Pro	Leu	Ser	Trp	Gly	Leu	Leu	Arg	His
225						230					235				240
Cys	His	Asp	Gly	Thr	Asn	Phe	Phe	Thr	Gly	Glu	Ala	Gly	Val	Arg	Leu
				245					250					255	
Asp	Tyr	Ile	Ser	Leu	His	Arg	Lys	Gly	Ala	Arg	Ser	Ser	Ile	Ser	Ile
			260					265					270		
Leu	Glu	Gln	Glu	Lys	Val	Val	Ala	Gln	Gln	Ile	Arg	Gln	Leu	Phe	Pro
		275					280					285			
Lys	Phe	Ala	Asp	Thr	Pro	Ile	Tyr	Asn	Asp	Glu	Ala	Asp	Pro	Leu	Val
	290					295					300				
Gly	Trp	Ser	Leu	Pro	Gln	Pro	Trp	Arg	Ala	Asp	Val	Thr	Tyr	Ala	Ala
305						310					315				320
Met	Val	Val	Lys	Val	Ile	Ala	Gln	His	Gln	Asn	Leu	Leu	Leu	Ala	Asn
				325					330					335	
Thr	Thr	Ser	Ala	Phe	Pro	Tyr	Ala	Leu	Leu	Ser	Asn	Asp	Asn	Ala	Phe
			340					345					350		
Leu	Ser	Tyr	His	Pro	His	Pro	Phe	Ala	Gln	Arg	Thr	Leu	Thr	Ala	Arg
		355					360					365			
Phe	Gln	Val	Asn	Asn	Thr	Arg	Pro	Pro	His	Val	Gln	Leu	Leu	Arg	Lys
	370					375					380				
Pro	Val	Leu	Thr	Ala	Met	Gly	Leu	Leu	Ala	Leu	Leu	Asp	Glu	Glu	Gln
385						390					395				400
Leu	Trp	Ala	Glu	Val	Ser	Gln	Ala	Gly	Thr	Val	Leu	Asp	Ser	Asn	His
				405					410					415	
Thr	Val	Gly	Val	Leu	Ala	Ser	Ala	His	Arg	Pro	Gln	Gly	Pro	Ala	Asp

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	420		425		430
Ala Trp Arg	Ala Ala Val	Leu Ile Tyr	Ala Ser Asp	Asp Thr Arg	Ala
	435		440		445
His Pro Asn	Arg Ser Val	Ala Val Thr	Leu Arg Leu	Arg Gly Val	Pro
	450		455		460
Pro Gly Pro	Gly Leu Val	Tyr Val Thr	Arg Tyr Leu	Asp Asn Gly	Leu
	465		470		480
Cys Ser Pro	Asp Gly Glu	Trp Arg Arg	Leu Gly Arg	Pro Val Phe	Pro
	485		490		495
Thr Ala Glu	Gln Phe Arg	Arg Met Arg	Ala Ala Glu	Asp Pro Val	Ala
	500		505		510
Ala Ala Pro	Arg Pro Leu	Pro Ala Gly	Gly Arg Leu	Thr Leu Arg	Pro
	515		520		525
Ala Leu Arg	Leu Pro Ser	Leu Leu Val	His Val Cys	Ala Arg Pro	
	530		535		540
Glu Lys Pro	Pro Gly Gln	Val Thr Arg	Leu Arg Ala	Leu Pro Leu	Thr
	545		550		560
Gln Gly Gln	Leu Val Leu	Val Trp Ser	Asp Glu His	Val Gly Ser	Lys
	565		570		575
Cys Leu Trp	Thr Tyr Glu	Ile Gln Phe	Ser Gln Asp	Gly Lys Ala	Tyr
	580		585		590
Thr Pro Val	Ser Arg Lys	Pro Ser Thr	Phe Asn Leu	Phe Val Phe	Ser
	595		600		605
Pro Asp Thr	Gly Ala Val	Ser Gly Ser	Tyr Arg Val	Arg Ala Leu	Asp
	610		615		620
Tyr Trp Ala	Arg Pro Gly	Pro Phe Ser	Asp Pro Val	Pro Tyr Leu	Glu
	625		630		640
Val Pro Val	Pro Arg Gly	Pro Pro Ser	Pro Gly Asn	Pro	
	645		650		

<210> 82
 <211> 153
 <212> PRT
 <213> Homo Sapiens

<400> 82

Met Gly Lys	Ile Ser Ser	Leu Pro Thr	Gln Leu Phe	Lys Cys Cys	Phe
1	5		10		15
Cys Asp Phe	Leu Lys Val	Lys Met His	Thr Met Ser	Ser Ser His	Leu
	20		25		30
Phe Tyr Leu	Ala Leu Cys	Leu Leu Thr	Phe Thr Ser	Ser Ala Thr	Ala
	35		40		45

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Gly Pro Glu Thr Leu Cys Gly Ala Glu Leu Val Asp Ala Leu Gln Phe
 50 55 60
 Val Cys Gly Asp Arg Gly Phe Tyr Phe Asn Lys Pro Thr Gly Tyr Gly
 65 70 75 80
 Ser Ser Ser Arg Arg Ala Pro Gln Thr Gly Ile Val Asp Glu Cys Cys
 85 90 95
 Phe Arg Ser Cys Asp Leu Arg Arg Leu Glu Met Tyr Cys Ala Pro Leu
 100 105 110
 Lys Pro Ala Lys Ser Ala Arg Ser Val Arg Ala Gln Arg His Thr Asp
 115 120 125
 Met Pro Lys Thr Gln Lys Glu Val His Leu Lys Asn Ala Ser Arg Gly
 130 135 140
 Ser Ala Gly Asn Lys Asn Tyr Arg Met
 145 150
 <210> 83
 <211> 1575
 <212> PRT
 <213> Homo Sapiens
 <400> 83
 Met Pro His Glu Glu Leu Pro Ser Leu Gln Arg Pro Arg Tyr Gly Ser
 1 5 10 15
 Ile Val Asp Asp Glu Arg Leu Ser Ala Glu Glu Met Asp Glu Arg Arg
 20 25 30
 Arg Gln Asn Ile Ala Tyr Glu Tyr Leu Cys His Leu Glu Glu Ala Lys
 35 40 45
 Arg Trp Met Glu Val Cys Leu Val Glu Glu Leu Pro Pro Thr Thr Glu
 50 55 60
 Leu Glu Glu Gly Leu Arg Asn Gly Val Tyr Leu Ala Lys Leu Ala Lys
 65 70 75 80
 Phe Phe Ala Pro Lys Met Val Ser Glu Lys Lys Ile Tyr Asp Val Glu
 85 90 95
 Gln Thr Arg Tyr Lys Lys Ser Gly Leu His Phe Arg His Thr Asp Asn
 100 105 110
 Thr Val Gln Trp Leu Arg Ala Met Glu Ser Ile Gly Leu Pro Lys Ile
 115 120 125
 Phe Tyr Pro Glu Thr Thr Asp Val Tyr Asp Arg Lys Asn Ile Pro Arg
 130 135 140
 Met Ile Tyr Cys Ile His Ala Leu Ser Leu Tyr Leu Phe Lys Leu Gly
 145 150 155 160
 Ile Ala Pro Gln Ile Gln Asp Leu Leu Gly Lys Val Asp Phe Thr Glu
 165 170 175

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Glu Glu Ile Ser Asn Met Arg Lys Glu Leu Glu Lys Tyr Gly Ile Gln
 180 185 190
 Met Pro Ser Phe Ser Lys Ile Gly Gly Ile Leu Ala Asn Glu Leu Ser
 195 200 205
 Val Asp Glu Ala Ala Leu His Ala Ala Val Ile Ala Ile Asn Glu Ala
 210 215 220
 Val Glu Lys Gly Ile Ala Glu Gln Thr Val Val Thr Leu Arg Asn Pro
 225 230 235 240
 Asn Ala Val Leu Thr Leu Val Asp Asp Asn Leu Ala Pro Glu Tyr Gln
 245 250 255
 Lys Glu Leu Trp Asp Ala Lys Lys Lys Lys Glu Glu Asn Ala Arg Leu
 260 265 270
 Lys Asn Ser Cys Ile Ser Glu Glu Glu Arg Asp Ala Tyr Glu Glu Leu
 275 280 285
 Leu Thr Gln Ala Glu Ile Gln Gly Asn Ile Asn Lys Val Asn Arg Gln
 290 295 300
 Ala Ala Val Asp His Ile Asn Ala Val Ile Pro Glu Gly Asp Pro Glu
 305 310 315 320
 Asn Thr Leu Leu Ala Leu Lys Lys Pro Glu Ala Gln Leu Pro Ala Val
 325 330 335
 Tyr Pro Phe Ala Ala Ala Met Tyr Gln Asn Glu Leu Phe Asn Leu Gln
 340 345 350
 Lys Gln Asn Thr Met Asn Tyr Leu Ala His Glu Glu Leu Leu Ile Ala
 355 360 365
 Val Glu Met Leu Ser Ala Val Ala Leu Leu Asn Gln Ala Leu Glu Ser
 370 375 380
 Asn Asp Leu Val Ser Val Gln Asn Gln Leu Arg Ser Pro Ala Ile Gly
 385 390 395 400
 Leu Asn Asn Leu Asp Lys Ala Tyr Val Glu Arg Tyr Ala Asn Thr Leu
 405 410 415
 Leu Ser Val Lys Leu Glu Val Leu Ser Gln Gly Gln Asp Asn Leu Ser
 420 425 430
 Trp Asn Glu Ile Gln Asn Cys Ile Asp Met Val Asn Ala Gln Ile Gln
 435 440 445
 Glu Glu Asn Asp Arg Val Val Ala Val Gly Tyr Ile Asn Glu Ala Ile
 450 455 460
 Asp Glu Gly Asn Pro Leu Arg Thr Leu Glu Thr Leu Leu Leu Pro Thr
 465 470 475 480
 Ala Asn Ile Ser Asp Val Asp Pro Ala His Ala Gln His Tyr Gln Asp
 485 490 495

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Val	Leu	Tyr	His	Ala	Lys	Ser	Gln	Lys	Leu	Gly	Asp	Ser	Glu	Ser	Val	500	505	510
Ser	Lys	Val	Leu	Trp	Leu	Asp	Glu	Ile	Gln	Gln	Ala	Val	Asp	Glu	Ala	515	520	525
Asn	Val	Asp	Glu	Asp	Arg	Ala	Lys	Gln	Trp	Val	Thr	Leu	Val	Val	Asp	530	535	540
Val	Asn	Gln	Cys	Leu	Glu	Gly	Lys	Lys	Ser	Ser	Asp	Ile	Leu	Ser	Val	545	550	555
Leu	Lys	Ser	Ser	Thr	Ser	Asn	Ala	Asn	Asp	Ile	Ile	Pro	Glu	Cys	Ala	565	570	575
Asp	Lys	Tyr	Tyr	Asp	Ala	Leu	Val	Lys	Ala	Lys	Glu	Leu	Lys	Ser	Glu	580	585	590
Arg	Val	Ser	Ser	Asp	Gly	Ser	Trp	Leu	Lys	Leu	Asn	Leu	His	Lys	Lys	595	600	605
Tyr	Asp	Tyr	Tyr	Tyr	Asn	Thr	Asp	Ser	Lys	Glu	Ser	Ser	Trp	Val	Thr	610	615	620
Pro	Glu	Ser	Cys	Phe	Tyr	Lys	Glu	Ser	Trp	Leu	Thr	Gly	Lys	Glu	Ile	625	630	635
Glu	Asp	Ile	Ile	Glu	Glu	Val	Thr	Val	Gly	Tyr	Ile	Arg	Glu	Asn	Ile	645	650	655
Trp	Ser	Ala	Ser	Glu	Glu	Leu	Leu	Leu	Arg	Phe	Gln	Ala	Thr	Ser	Ser	660	665	670
Gly	Pro	Ile	Leu	Arg	Glu	Glu	Phe	Glu	Ala	Arg	Lys	Ser	Phe	Leu	His	675	680	685
Glu	Gln	Glu	Glu	Asn	Val	Val	Lys	Ile	Gln	Ala	Phe	Trp	Lys	Gly	Tyr	690	695	700
Lys	Gln	Arg	Lys	Glu	Tyr	Met	His	Arg	Arg	Gln	Thr	Phe	Ile	Asp	Asn	705	710	715
Thr	Asp	Ser	Val	Val	Lys	Ile	Gln	Ser	Trp	Phe	Arg	Met	Ala	Thr	Ala	725	730	735
Arg	Lys	Ser	Tyr	Leu	Ser	Arg	Leu	Gln	Tyr	Phe	Arg	Asp	His	Asn	Asn	740	745	750
Glu	Ile	Val	Lys	Ile	Gln	Ser	Leu	Leu	Arg	Ala	Asn	Lys	Ala	Arg	Asp	755	760	765
Asp	Tyr	Lys	Thr	Leu	Val	Gly	Ser	Glu	Asn	Pro	Pro	Leu	Thr	Val	Ile	770	775	780
Arg	Lys	Phe	Val	Tyr	Leu	Leu	Asp	Gln	Ser	Asp	Leu	Asp	Phe	Gln	Glu	785	790	795
Glu	Leu	Glu	Val	Ala	Arg	Leu	Arg	Glu	Glu	Val	Val	Thr	Lys	Ile	Arg	805	810	815

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Ala Asn Gln Gln Leu Glu Lys Asp Leu Asn Leu Met Asp Ile Lys Ile
 820 825 830

Gly Leu Leu Val Lys Asn Arg Ile Thr Leu Glu Asp Val Ile Ser His
 835 840 845

Ser Lys Lys Leu Asn Lys Lys Lys Gly Gly Glu Met Glu Ile Leu Asn
 850 855 860

Asn Thr Asp Asn Gln Gly Ile Lys Ser Leu Ser Lys Glu Arg Arg Lys
 865 870 875 880

Thr Leu Glu Thr Tyr Gln Gln Leu Phe Tyr Leu Leu Gln Thr Asn Pro
 885 890 895

Leu Tyr Leu Ala Lys Leu Ile Phe Gln Met Pro Gln Asn Lys Ser Thr
 900 905 910

Lys Phe Met Asp Thr Val Ile Phe Thr Leu Tyr Asn Tyr Ala Ser Asn
 915 920 925

Gln Arg Glu Glu Tyr Leu Leu Leu Lys Leu Phe Lys Thr Ala Leu Glu
 930 935 940

Glu Glu Ile Lys Ser Lys Val Asp Gln Val Gln Asp Ile Val Thr Gly
 945 950 955 960

Asn Pro Thr Val Ile Lys Met Val Val Ser Phe Asn Arg Gly Ala Arg
 965 970 975

Gly Gln Asn Thr Leu Arg Gln Leu Leu Ala Pro Val Val Lys Glu Ile
 980 985 990

Ile Asp Asp Lys Ser Leu Ile Ile Asn Thr Asn Pro Val Glu Val Tyr
 995 1000 1005

Lys Ala Trp Val Asn Gln Leu Glu Thr Gln Thr Gly Glu Ala Ser
 1010 1015 1020

Lys Leu Pro Tyr Asp Val Thr Thr Glu Gln Ala Leu Thr Tyr Pro
 1025 1030 1035

Glu Val Lys Asn Lys Leu Glu Ala Ser Ile Glu Asn Leu Arg Arg
 1040 1045 1050

Val Thr Asp Lys Val Leu Asn Ser Ile Ile Ser Ser Leu Asp Leu
 1055 1060 1065

Leu Pro Tyr Gly Leu Arg Tyr Ile Ala Lys Val Leu Lys Asn Ser
 1070 1075 1080

Ile His Glu Lys Phe Pro Asp Ala Thr Glu Asp Glu Leu Leu Lys
 1085 1090 1095

Ile Val Gly Asn Leu Leu Tyr Tyr Arg Tyr Met Asn Pro Ala Ile
 1100 1105 1110

Val Ala Pro Asp Gly Phe Asp Ile Ile Asp Met Thr Ala Gly Gly
 1115 1120 1125

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Gln Ile	Asn Ser Asp	Gln Arg	Arg Asn Leu Gly	Ser Val Ala Lys
1130		1135		1140
Val Leu	Gln His Ala Ala	Ser Asn Lys Leu Phe	Glu Gly Glu Asn	
1145		1150	1155	
Glu His	Leu Ser Ser Met	Asn Asn Tyr Leu Ser	Glu Thr Tyr Gln	
1160		1165	1170	
Glu Phe	Arg Lys Tyr Phe	Lys Glu Ala Cys Asn	Val Pro Glu Pro	
1175		1180	1185	
Glu Glu	Lys Phe Asn Met	Asp Lys Tyr Thr Asp	Leu Val Thr Val	
1190		1195	1200	
Ser Lys	Pro Val Ile Tyr	Ile Ser Ile Glu Glu	Ile Ile Ser Thr	
1205		1210	1215	
His Ser	Leu Leu Leu Glu	His Gln Asp Ala Ile	Ala Pro Glu Lys	
1220		1225	1230	
Asn Asp	Leu Leu Ser Glu	Leu Leu Gly Ser Leu	Gly Glu Val Pro	
1235		1240	1245	
Thr Val	Glu Ser Phe Leu	Gly Glu Gly Ala Val	Asp Pro Asn Asp	
1250		1255	1260	
Pro Asn	Lys Ala Asn Thr	Leu Ser Gln Leu Ser	Lys Thr Glu Ile	
1265		1270	1275	
Ser Leu	Val Leu Thr Ser	Lys Tyr Asp Ile Glu	Asp Gly Glu Ala	
1280		1285	1290	
Ile Asp	Ser Arg Ser Leu	Met Ile Lys Thr Lys	Lys Leu Ile Ile	
1295		1300	1305	
Asp Val	Ile Arg Asn Gln	Pro Gly Asn Thr Leu	Thr Glu Ile Leu	
1310		1315	1320	
Glu Thr	Pro Ala Thr Ala	Gln Gln Glu Val Asp	His Ala Thr Asp	
1325		1330	1335	
Met Val	Ser Arg Ala Met	Ile Asp Ser Arg Thr	Pro Glu Glu Met	
1340		1345	1350	
Lys His	Ser Gln Ser Met	Ile Glu Asp Ala Gln	Leu Pro Leu Glu	
1355		1360	1365	
Gln Lys	Lys Arg Lys Ile	Gln Arg Asn Leu Arg	Thr Leu Glu Gln	
1370		1375	1380	
Thr Gly	His Val Ser Ser	Glu Asn Lys Tyr Gln	Asp Ile Leu Asn	
1385		1390	1395	
Glu Ile	Ala Lys Asp Ile	Arg Asn Gln Arg Ile	Tyr Arg Lys Leu	
1400		1405	1410	
Arg Lys	Ala Glu Leu Ala	Lys Leu Gln Gln Thr	Leu Asn Ala Leu	
1415		1420	1425	

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Asn Lys Lys Ala Ala Phe Tyr Glu Glu Gln Ile Asn Tyr Tyr Asp
 1430 1435 1440
 Thr Tyr Ile Lys Thr Cys Leu Asp Asn Leu Lys Arg Lys Asn Thr
 1445 1450 1455
 Arg Arg Ser Ile Lys Leu Asp Gly Lys Gly Glu Pro Lys Gly Ala
 1460 1465 1470
 Lys Arg Ala Lys Pro Val Lys Tyr Thr Ala Ala Lys Leu His Glu
 1475 1480 1485
 Lys Gly Val Leu Leu Asp Ile Asp Asp Leu Gln Thr Asn Gln Phe
 1490 1495 1500
 Lys Asn Val Thr Phe Asp Ile Ile Ala Thr Glu Asp Val Gly Ile
 1505 1510 1515
 Phe Asp Val Arg Ser Lys Phe Leu Gly Val Glu Met Glu Lys Val
 1520 1525 1530
 Gln Leu Asn Ile Gln Asp Leu Leu Gln Met Gln Tyr Glu Gly Val
 1535 1540 1545
 Ala Val Met Lys Met Phe Asp Lys Val Lys Val Asn Val Asn Leu
 1550 1555 1560
 Leu Ile Tyr Leu Leu Asn Lys Lys Phe Tyr Gly Lys
 1565 1570 1575
 <210> 84
 <211> 165
 <212> PRT
 <213> Homo Sapiens
 <400> 84
 Met Gly Trp Asp Leu Thr Val Lys Met Leu Ala Gly Asn Glu Phe Gln
 1 5 10 15
 Val Ser Leu Ser Ser Ser Met Ser Val Ser Glu Leu Lys Ala Gln Ile
 20 25 30
 Thr Gln Lys Ile Gly Val His Ala Phe Gln Gln Arg Leu Ala Val His
 35 40 45
 Pro Ser Gly Val Ala Leu Gln Asp Arg Val Pro Leu Ala Ser Gln Gly
 50 55 60
 Leu Gly Pro Gly Ser Thr Val Leu Leu Val Val Asp Lys Cys Asp Glu
 65 70 75 80
 Pro Leu Ser Ile Leu Val Arg Asn Asn Lys Gly Arg Ser Ser Thr Tyr
 85 90 95
 Glu Val Arg Leu Thr Gln Thr Val Ala His Leu Lys Gln Gln Val Ser
 100 105 110
 Gly Leu Glu Gly Val Gln Asp Asp Leu Phe Trp Leu Thr Phe Glu Gly

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115	120	125
Lys Pro Leu Glu Asp Gln Leu Pro Leu Gly Glu Tyr Gly Leu Lys Pro		
130	135	140
Leu Ser Thr Val Phe Met Asn Leu Arg Leu Arg Gly Gly Gly Thr Glu		
145	150	155
Pro Gly Gly Arg Ser		
	165	

<210> 85
 <211> 1218
 <212> PRT
 <213> Homo Sapiens

<400> 85

Met Arg Ser Pro Arg Thr Arg Gly Arg Ser Gly Arg Pro Leu Ser Leu		
1	5	10
Leu Leu Ala Leu Leu Cys Ala Leu Arg Ala Lys Val Cys Gly Ala Ser		
	20	25
Gly Gln Phe Glu Leu Glu Ile Leu Ser Met Gln Asn Val Asn Gly Glu		
	35	40
Leu Gln Asn Gly Asn Cys Cys Gly Gly Ala Arg Asn Pro Gly Asp Arg		
	50	55
Lys Cys Thr Arg Asp Glu Cys Asp Thr Tyr Phe Lys Val Cys Leu Lys		
65	70	75
Glu Tyr Gln Ser Arg Val Thr Ala Gly Gly Pro Cys Ser Phe Gly Ser		
	85	90
Gly Ser Thr Pro Val Ile Gly Gly Asn Thr Phe Asn Leu Lys Ala Ser		
	100	105
Arg Gly Asn Asp Pro Asn Arg Ile Val Leu Pro Phe Ser Phe Ala Trp		
	115	120
Pro Arg Ser Tyr Thr Leu Leu Val Glu Ala Trp Asp Ser Ser Asn Asp		
	130	135
Thr Val Gln Pro Asp Ser Ile Ile Glu Lys Ala Ser His Ser Gly Met		
145	150	155
Ile Asn Pro Ser Arg Gln Trp Gln Thr Leu Lys Gln Asn Thr Gly Val		
	165	170
Ala His Phe Glu Tyr Gln Ile Arg Val Thr Cys Asp Asp Tyr Tyr Tyr		
	180	185
Gly Phe Gly Cys Asn Lys Phe Cys Arg Pro Arg Asp Asp Phe Phe Gly		
	195	200
His Tyr Ala Cys Asp Gln Asn Gly Asn Lys Thr Cys Met Glu Gly Trp		
	210	215
		220

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Met	Gly	Pro	Glu	Cys	Asn	Arg	Ala	Ile	Cys	Arg	Gln	Gly	Cys	Ser	Pro	225	230	235	240
Lys	His	Gly	Ser	Cys	Lys	Leu	Pro	Gly	Asp	Cys	Arg	Cys	Gln	Tyr	Gly	245	250	255	
Trp	Gln	Gly	Leu	Tyr	Cys	Asp	Lys	Cys	Ile	Pro	His	Pro	Gly	Cys	Val	260	265	270	
His	Gly	Ile	Cys	Asn	Glu	Pro	Trp	Gln	Cys	Leu	Cys	Glu	Thr	Asn	Trp	275	280	285	
Gly	Gly	Gln	Leu	Cys	Asp	Lys	Asp	Leu	Asn	Tyr	Cys	Gly	Thr	His	Gln	290	295	300	
Pro	Cys	Leu	Asn	Gly	Gly	Thr	Cys	Ser	Asn	Thr	Gly	Pro	Asp	Lys	Tyr	305	310	315	320
Gln	Cys	Ser	Cys	Pro	Glu	Gly	Tyr	Ser	Gly	Pro	Asn	Cys	Glu	Ile	Ala	325	330		335
Glu	His	Ala	Cys	Leu	Ser	Asp	Pro	Cys	His	Asn	Arg	Gly	Ser	Cys	Lys	340	345	350	
Glu	Thr	Ser	Leu	Gly	Phe	Glu	Cys	Glu	Cys	Ser	Pro	Gly	Trp	Thr	Gly	355	360	365	
Pro	Thr	Cys	Ser	Thr	Asn	Ile	Asp	Asp	Cys	Ser	Pro	Asn	Asn	Cys	Ser	370	375	380	
His	Gly	Gly	Thr	Cys	Gln	Asp	Leu	Val	Asn	Gly	Phe	Lys	Cys	Val	Cys	385	390	395	400
Pro	Pro	Gln	Trp	Thr	Gly	Lys	Thr	Cys	Gln	Leu	Asp	Ala	Asn	Glu	Cys	405	410		415
Glu	Ala	Lys	Pro	Cys	Val	Asn	Ala	Lys	Ser	Cys	Lys	Asn	Leu	Ile	Ala	420	425		430
Ser	Tyr	Tyr	Cys	Asp	Cys	Leu	Pro	Gly	Trp	Met	Gly	Gln	Asn	Cys	Asp	435	440	445	
Ile	Asn	Ile	Asn	Asp	Cys	Leu	Gly	Gln	Cys	Gln	Asn	Asp	Ala	Ser	Cys	450	455	460	
Arg	Asp	Leu	Val	Asn	Gly	Tyr	Arg	Cys	Ile	Cys	Pro	Pro	Gly	Tyr	Ala	465	470	475	480
Gly	Asp	His	Cys	Glu	Arg	Asp	Ile	Asp	Glu	Cys	Ala	Ser	Asn	Pro	Cys	485	490		495
Leu	Asn	Gly	Gly	His	Cys	Gln	Asn	Glu	Ile	Asn	Arg	Phe	Gln	Cys	Leu	500	505	510	
Cys	Pro	Thr	Gly	Phe	Ser	Gly	Asn	Leu	Cys	Gln	Leu	Asp	Ile	Asp	Tyr	515	520	525	
Cys	Glu	Pro	Asn	Pro	Cys	Gln	Asn	Gly	Ala	Gln	Cys	Tyr	Asn	Arg	Ala	530	535	540	

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Ser Asp Tyr Phe Cys Lys Cys Pro Glu Asp Tyr Glu Gly Lys Asn Cys
 545 550 555 560
 Ser His Leu Lys Asp His Cys Arg Thr Thr Pro Cys Glu Val Ile Asp
 565 570 575
 Ser Cys Thr Val Ala Met Ala Ser Asn Asp Thr Pro Glu Gly Val Arg
 580 585 590
 Tyr Ile Ser Ser Asn Val Cys Gly Pro His Gly Lys Cys Lys Ser Gln
 595 600 605
 Ser Gly Gly Lys Phe Thr Cys Asp Cys Asn Lys Gly Phe Thr Gly Thr
 610 615 620
 Tyr Cys His Glu Asn Ile Asn Asp Cys Glu Ser Asn Pro Cys Arg Asn
 625 630 635 640
 Gly Gly Thr Cys Ile Asp Gly Val Asn Ser Tyr Lys Cys Ile Cys Ser
 645 650 655
 Asp Gly Trp Glu Gly Ala Tyr Cys Glu Thr Asn Ile Asn Asp Cys Ser
 660 665 670
 Gln Asn Pro Cys His Asn Gly Gly Thr Cys Arg Asp Leu Val Asn Asp
 675 680 685
 Phe Tyr Cys Asp Cys Lys Asn Gly Trp Lys Gly Lys Thr Cys His Ser
 690 695 700
 Arg Asp Ser Gln Cys Asp Glu Ala Thr Cys Asn Asn Gly Gly Thr Cys
 705 710 715 720
 Tyr Asp Glu Gly Asp Ala Phe Lys Cys Met Cys Pro Gly Gly Trp Glu
 725 730 735
 Gly Thr Thr Cys Asn Ile Ala Arg Asn Ser Ser Cys Leu Pro Asn Pro
 740 745 750
 Cys His Asn Gly Gly Thr Cys Val Val Asn Gly Glu Ser Phe Thr Cys
 755 760 765
 Val Cys Lys Glu Gly Trp Glu Gly Pro Ile Cys Ala Gln Asn Thr Asn
 770 775 780
 Asp Cys Ser Pro His Pro Cys Tyr Asn Ser Gly Thr Cys Val Asp Gly
 785 790 795 800
 Asp Asn Trp Tyr Arg Cys Glu Cys Ala Pro Gly Phe Ala Gly Pro Asp
 805 810 815
 Cys Arg Ile Asn Ile Asn Glu Cys Gln Ser Ser Pro Cys Ala Phe Gly
 820 825 830
 Ala Thr Cys Val Asp Glu Ile Asn Gly Tyr Arg Cys Val Cys Pro Pro
 835 840 845
 Gly His Ser Gly Ala Lys Cys Gln Glu Val Ser Gly Arg Pro Cys Ile
 850 855 860

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Thr Met Gly Ser Val Ile Pro Asp Gly Ala Lys Trp Asp Asp Asp Cys
 865 870 875 880
 Asn Thr Cys Gln Cys Leu Asn Gly Arg Ile Ala Cys Ser Lys Val Trp
 885 890 895
 Cys Gly Pro Arg Pro Cys Leu Leu His Lys Gly His Ser Glu Cys Pro
 900 905 910
 Ser Gly Gln Ser Cys Ile Pro Ile Leu Asp Asp Gln Cys Phe Val His
 915 920 925
 Pro Cys Thr Gly Val Gly Glu Cys Arg Ser Ser Ser Leu Gln Pro Val
 930 935 940
 Lys Thr Lys Cys Thr Ser Asp Ser Tyr Tyr Gln Asp Asn Cys Ala Asn
 945 950 955 960
 Ile Thr Phe Thr Phe Asn Lys Glu Met Met Ser Pro Gly Leu Thr Thr
 965 970 975
 Glu His Ile Cys Ser Glu Leu Arg Asn Leu Asn Ile Leu Lys Asn Val
 980 985 990
 Ser Ala Glu Tyr Ser Ile Tyr Ile Ala Cys Glu Pro Ser Pro Ser Ala
 995 1000 1005
 Asn Asn Glu Ile His Val Ala Ile Ser Ala Glu Asp Ile Arg Asp
 1010 1015 1020
 Asp Gly Asn Pro Ile Lys Glu Ile Thr Asp Lys Ile Ile Asp Leu
 1025 1030 1035
 Val Ser Lys Arg Asp Gly Asn Ser Ser Leu Ile Ala Ala Val Ala
 1040 1045 1050
 Glu Val Arg Val Gln Arg Arg Pro Leu Lys Asn Arg Thr Asp Phe
 1055 1060 1065
 Leu Val Pro Leu Leu Ser Ser Val Leu Thr Val Ala Trp Ile Cys
 1070 1075 1080
 Cys Leu Val Thr Ala Phe Tyr Trp Cys Leu Arg Lys Arg Arg Lys
 1085 1090 1095
 Pro Gly Ser His Thr His Ser Ala Ser Glu Asp Asn Thr Thr Asn
 1100 1105 1110
 Asn Val Arg Glu Gln Leu Asn Gln Ile Lys Asn Pro Ile Glu Lys
 1115 1120 1125
 His Gly Ala Asn Thr Val Pro Ile Lys Asp Tyr Glu Asn Lys Asn
 1130 1135 1140
 Ser Lys Met Ser Lys Ile Arg Thr His Asn Ser Glu Val Glu Glu
 1145 1150 1155
 Asp Asp Met Asp Lys His Gln Gln Lys Ala Arg Phe Ala Lys Gln
 1160 1165 1170

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Pro Ala Tyr Thr Leu Val Asp Arg Glu Glu Lys Pro Pro Asn Gly
 1175 1180 1185

Thr Pro Thr Lys His Pro Asn Trp Thr Asn Lys Gln Asp Asn Arg
 1190 1195 1200

Asp Leu Glu Ser Ala Gln Ser Leu Asn Arg Met Glu Tyr Ile Val
 1205 1210 1215

<210> 86

<211> 3110

<212> PRT

<213> Homo Sapiens

<400> 86

Met Pro Gly Ala Ala Gly Val Leu Leu Leu Leu Leu Ser Gly Gly
 1 5 10 15

Leu Gly Gly Val Gln Ala Gln Arg Pro Gln Gln Gln Arg Gln Ser Gln
 20 25 30

Ala His Gln Gln Arg Gly Leu Phe Pro Ala Val Leu Asn Leu Ala Ser
 35 40 45

Asn Ala Leu Ile Thr Thr Asn Ala Thr Cys Gly Glu Lys Gly Pro Glu
 50 55 60

Met Tyr Cys Lys Leu Val Glu His Val Pro Gly Gln Pro Val Arg Asn
 65 70 75 80

Pro Gln Cys Arg Ile Cys Asn Gln Asn Ser Ser Asn Pro Asn Gln Arg
 85 90 95

His Pro Ile Thr Asn Ala Ile Asp Gly Lys Asn Thr Trp Trp Gln Ser
 100 105 110

Pro Ser Ile Lys Asn Gly Ile Glu Tyr His Tyr Val Thr Ile Thr Leu
 115 120 125

Asp Leu Gln Gln Val Phe Gln Ile Ala Tyr Val Ile Val Lys Ala Ala
 130 135 140

Asn Ser Pro Arg Pro Gly Asn Trp Ile Leu Glu Arg Ser Leu Asp Asp
 145 150 155 160

Val Glu Tyr Lys Pro Trp Gln Tyr His Ala Val Thr Asp Thr Glu Cys
 165 170 175

Leu Thr Leu Tyr Asn Ile Tyr Pro Arg Thr Gly Pro Pro Ser Tyr Ala
 180 185 190

Lys Asp Asp Glu Val Ile Cys Thr Ser Phe Tyr Ser Lys Ile His Pro
 195 200 205

Leu Glu Asn Gly Glu Ile His Ile Ser Leu Ile Asn Gly Arg Pro Ser
 210 215 220

Ala Asp Asp Pro Ser Pro Glu Leu Leu Glu Phe Thr Ser Ala Arg Tyr
 225 230 235 240

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Ile Arg Leu Arg Phe Gln Arg Ile Arg Thr Leu Asn Ala Asp Leu Met
 245 250 255
 Met Phe Ala His Lys Asp Pro Arg Glu Ile Asp Pro Ile Val Thr Arg
 260 265 270
 Arg Tyr Tyr Tyr Ser Val Lys Asp Ile Ser Val Gly Gly Met Cys Ile
 275 280 285
 Cys Tyr Gly His Ala Arg Ala Cys Pro Leu Asp Pro Ala Thr Asn Lys
 290 295 300
 Ser Arg Cys Glu Cys Glu His Asn Thr Cys Gly Asp Ser Cys Asp Gln
 305 310 315 320
 Cys Cys Pro Gly Phe His Gln Lys Pro Trp Arg Ala Gly Thr Phe Leu
 325 330 335
 Thr Lys Thr Glu Cys Glu Ala Cys Asn Cys His Gly Lys Ala Glu Glu
 340 345 350
 Cys Tyr Tyr Asp Glu Asn Val Ala Arg Arg Asn Leu Ser Leu Asn Ile
 355 360 365
 Arg Gly Lys Tyr Ile Gly Gly Gly Val Cys Ile Asn Cys Thr Gln Asn
 370 375 380
 Thr Ala Gly Ile Asn Cys Glu Thr Cys Thr Asp Gly Phe Phe Arg Pro
 385 390 395 400
 Lys Gly Val Ser Pro Asn Tyr Pro Arg Pro Cys Gln Pro Cys His Cys
 405 410 415
 Asp Pro Ile Gly Ser Leu Asn Glu Val Cys Val Lys Asp Glu Lys His
 420 425 430
 Ala Arg Arg Gly Leu Ala Pro Gly Ser Cys His Cys Lys Thr Gly Phe
 435 440 445
 Gly Gly Val Ser Cys Asp Arg Cys Ala Arg Gly Tyr Thr Gly Tyr Pro
 450 455 460
 Asp Cys Lys Ala Cys Asn Cys Ser Gly Leu Gly Ser Lys Asn Glu Asp
 465 470 475 480
 Pro Cys Phe Gly Pro Cys Ile Cys Lys Glu Asn Val Glu Gly Gly Asp
 485 490 495
 Cys Ser Arg Cys Lys Ser Gly Phe Phe Asn Leu Gln Glu Asp Asn Trp
 500 505 510
 Lys Gly Cys Asp Glu Cys Phe Cys Ser Gly Val Ser Asn Arg Cys Gln
 515 520 525
 Ser Ser Tyr Trp Thr Tyr Gly Lys Ile Gln Asp Met Ser Gly Trp Tyr
 530 535 540
 Leu Thr Asp Leu Pro Gly Arg Ile Arg Val Ala Pro Gln Gln Asp Asp
 545 550 555 560

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Leu	Asp	Ser	Pro	Gln	Gln	Ile	Ser	Ile	Ser	Asn	Ala	Glu	Ala	Arg	Gln	
				565					570					575		
Ala	Leu	Pro	His	Ser	Tyr	Tyr	Trp	Ser	Ala	Pro	Ala	Pro	Tyr	Leu	Gly	
			580					585					590			
Asn	Lys	Leu	Pro	Ala	Val	Gly	Gly	Gln	Leu	Thr	Phe	Thr	Ile	Ser	Tyr	
		595					600					605				
Asp	Leu	Glu	Glu	Glu	Glu	Glu	Asp	Thr	Glu	Arg	Val	Leu	Gln	Leu	Met	
	610					615					620					
Ile	Ile	Leu	Glu	Gly	Asn	Asp	Leu	Ser	Ile	Ser	Thr	Ala	Gln	Asp	Glu	
625					630					635					640	
Val	Tyr	Leu	His	Pro	Ser	Glu	Glu	His	Thr	Asn	Val	Leu	Leu	Leu	Lys	
			645						650					655		
Glu	Glu	Ser	Phe	Thr	Ile	His	Gly	Thr	His	Phe	Pro	Val	Arg	Arg	Lys	
			660					665					670			
Glu	Phe	Met	Thr	Val	Leu	Ala	Asn	Leu	Lys	Arg	Val	Leu	Leu	Gln	Ile	
	675						680					685				
Thr	Tyr	Ser	Phe	Gly	Met	Asp	Ala	Ile	Phe	Arg	Leu	Ser	Ser	Val	Asn	
	690					695					700					
Leu	Glu	Ser	Ala	Val	Ser	Tyr	Pro	Thr	Asp	Gly	Ser	Ile	Ala	Ala	Ala	
705					710					715					720	
Val	Glu	Val	Cys	Gln	Cys	Pro	Pro	Gly	Tyr	Thr	Gly	Ser	Ser	Cys	Glu	
			725						730					735		
Ser	Cys	Trp	Pro	Arg	His	Arg	Arg	Val	Asn	Gly	Thr	Ile	Phe	Gly	Gly	
			740					745					750			
Ile	Cys	Glu	Pro	Cys	Gln	Cys	Phe	Gly	His	Ala	Glu	Ser	Cys	Asp	Asp	
	755						760					765				
Val	Thr	Gly	Glu	Cys	Leu	Asn	Cys	Lys	Asp	His	Thr	Gly	Gly	Pro	Tyr	
	770					775					780					
Cys	Asp	Lys	Cys	Leu	Pro	Gly	Phe	Tyr	Gly	Glu	Pro	Thr	Lys	Gly	Thr	
785					790					795					800	
Ser	Glu	Asp	Cys	Gln	Pro	Cys	Ala	Cys	Pro	Leu	Asn	Ile	Pro	Ser	Asn	
			805						810					815		
Asn	Phe	Ser	Pro	Thr	Cys	His	Leu	Asp	Arg	Ser	Leu	Gly	Leu	Ile	Cys	
			820					825					830			
Asp	Gly	Cys	Pro	Val	Gly	Tyr	Thr	Gly	Pro	Arg	Cys	Glu	Arg	Cys	Ala	
	835						840					845				
Glu	Gly	Tyr	Phe	Gly	Gln	Pro	Ser	Val	Pro	Gly	Gly	Ser	Cys	Gln	Pro	
	850					855					860					
Cys	Gln	Cys	Asn	Asp	Asn	Leu	Asp	Phe	Ser	Ile	Pro	Gly	Ser	Cys	Asp	
865					870					875					880	

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Ser Leu Ser Gly Ser Cys Leu Ile Cys Lys Pro Gly Thr Thr Gly Arg
 885 890 895
 Tyr Cys Glu Leu Cys Ala Asp Gly Tyr Phe Gly Asp Ala Val Asp Ala
 900 905 910
 Lys Asn Cys Gln Pro Cys Arg Cys Asn Ala Gly Gly Ser Phe Ser Glu
 915 920 925
 Val Cys His Ser Gln Thr Gly Gln Cys Glu Cys Arg Ala Asn Val Gln
 930 935 940
 Gly Gln Arg Cys Asp Lys Cys Lys Ala Gly Thr Phe Gly Leu Gln Ser
 945 950 955 960
 Ala Arg Gly Cys Val Pro Cys Asn Cys Asn Ser Phe Gly Ser Lys Ser
 965 970 975
 Phe Asp Cys Glu Glu Ser Gly Gln Cys Trp Cys Gln Pro Gly Val Thr
 980 985 990
 Gly Lys Lys Cys Asp Arg Cys Ala His Gly Tyr Phe Asn Phe Gln Glu
 995 1000 1005
 Gly Gly Cys Thr Ala Cys Glu Cys Ser His Leu Gly Asn Asn Cys
 1010 1015 1020
 Asp Pro Lys Thr Gly Arg Cys Ile Cys Pro Pro Asn Thr Ile Gly
 1025 1030 1035
 Glu Lys Cys Ser Lys Cys Ala Pro Asn Thr Trp Gly His Ser Ile
 1040 1045 1050
 Thr Thr Gly Cys Lys Ala Cys Asn Cys Ser Thr Val Gly Ser Leu
 1055 1060 1065
 Asp Phe Gln Cys Asn Val Asn Thr Gly Gln Cys Asn Cys His Pro
 1070 1075 1080
 Lys Phe Ser Gly Ala Lys Cys Thr Glu Cys Ser Arg Gly His Trp
 1085 1090 1095
 Asn Tyr Pro Arg Cys Asn Leu Cys Asp Cys Phe Leu Pro Gly Thr
 1100 1105 1110
 Asp Ala Thr Thr Cys Asp Ser Glu Thr Lys Lys Cys Ser Cys Ser
 1115 1120 1125
 Asp Gln Thr Gly Gln Cys Thr Cys Lys Val Asn Val Glu Gly Ile
 1130 1135 1140
 His Cys Asp Arg Cys Arg Pro Gly Lys Phe Gly Leu Asp Ala Lys
 1145 1150 1155
 Asn Pro Leu Gly Cys Ser Ser Cys Tyr Cys Phe Gly Thr Thr Thr
 1160 1165 1170
 Gln Cys Ser Glu Ala Lys Gly Leu Ile Arg Thr Trp Val Thr Leu
 1175 1180 1185

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Lys	Ala	Glu	Gln	Thr	Ile	Leu	Pro	Leu	Val	Asp	Glu	Ala	Leu	Gln
1190						1195					1200			
His	Thr	Thr	Thr	Lys	Gly	Ile	Val	Phe	Gln	His	Pro	Glu	Ile	Val
1205						1210					1215			
Ala	His	Met	Asp	Leu	Met	Arg	Glu	Asp	Leu	His	Leu	Glu	Pro	Phe
1220						1225					1230			
Tyr	Trp	Lys	Leu	Pro	Glu	Gln	Phe	Glu	Gly	Lys	Lys	Leu	Met	Ala
1235						1240					1245			
Tyr	Gly	Gly	Lys	Leu	Lys	Tyr	Ala	Ile	Tyr	Phe	Glu	Ala	Arg	Glu
1250						1255					1260			
Glu	Thr	Gly	Phe	Ser	Thr	Tyr	Asn	Pro	Gln	Val	Ile	Ile	Arg	Gly
1265						1270					1275			
Gly	Thr	Pro	Thr	His	Ala	Arg	Ile	Ile	Val	Arg	His	Met	Ala	Ala
1280						1285					1290			
Pro	Leu	Ile	Gly	Gln	Leu	Thr	Arg	His	Glu	Ile	Glu	Met	Thr	Glu
1295						1300					1305			
Lys	Glu	Trp	Lys	Tyr	Tyr	Gly	Asp	Asp	Pro	Arg	Val	His	Arg	Thr
1310						1315					1320			
Val	Thr	Arg	Glu	Asp	Phe	Leu	Asp	Ile	Leu	Tyr	Asp	Ile	His	Tyr
1325						1330					1335			
Ile	Leu	Ile	Lys	Ala	Thr	Tyr	Gly	Asn	Phe	Met	Arg	Gln	Ser	Arg
1340						1345					1350			
Ile	Ser	Glu	Ile	Ser	Met	Glu	Val	Ala	Glu	Gln	Gly	Arg	Gly	Thr
1355						1360					1365			
Thr	Met	Thr	Pro	Pro	Ala	Asp	Leu	Ile	Glu	Lys	Cys	Asp	Cys	Pro
1370						1375					1380			
Leu	Gly	Tyr	Ser	Gly	Leu	Ser	Cys	Glu	Ala	Cys	Leu	Pro	Gly	Phe
1385						1390					1395			
Tyr	Arg	Leu	Arg	Ser	Gln	Pro	Gly	Gly	Arg	Thr	Pro	Gly	Pro	Thr
1400						1405					1410			
Leu	Gly	Thr	Cys	Val	Pro	Cys	Gln	Cys	Asn	Gly	His	Ser	Ser	Leu
1415						1420					1425			
Cys	Asp	Pro	Glu	Thr	Ser	Ile	Cys	Gln	Asn	Cys	Gln	His	His	Thr
1430						1435					1440			
Ala	Gly	Asp	Phe	Cys	Glu	Arg	Cys	Ala	Leu	Gly	Tyr	Tyr	Gly	Ile
1445						1450					1455			
Val	Lys	Gly	Leu	Pro	Asn	Asp	Cys	Gln	Gln	Cys	Ala	Cys	Pro	Leu
1460						1465					1470			
Ile	Ser	Ser	Ser	Asn	Asn	Phe	Ser	Pro	Ser	Cys	Val	Ala	Glu	Gly
1475						1480					1485			

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Leu	Asp	Asp	Tyr	Arg	Cys	Thr	Ala	Cys	Pro	Arg	Gly	Tyr	Glu	Gly
1490						1495					1500			
Gln	Tyr	Cys	Glu	Arg	Cys	Ala	Pro	Gly	Tyr	Thr	Gly	Ser	Pro	Gly
1505						1510					1515			
Asn	Pro	Gly	Gly	Ser	Cys	Gln	Glu	Cys	Glu	Cys	Asp	Pro	Tyr	Gly
1520						1525					1530			
Ser	Leu	Pro	Val	Pro	Cys	Asp	Pro	Val	Thr	Gly	Phe	Cys	Thr	Cys
1535						1540					1545			
Arg	Pro	Gly	Ala	Thr	Gly	Arg	Lys	Cys	Asp	Gly	Cys	Lys	His	Trp
1550						1555					1560			
His	Ala	Arg	Glu	Gly	Trp	Glu	Cys	Val	Phe	Cys	Gly	Asp	Glu	Cys
1565						1570					1575			
Thr	Gly	Leu	Leu	Leu	Gly	Asp	Leu	Ala	Arg	Leu	Glu	Gln	Met	Val
1580						1585					1590			
Met	Ser	Ile	Asn	Leu	Thr	Gly	Pro	Leu	Pro	Ala	Pro	Tyr	Lys	Met
1595						1600					1605			
Leu	Tyr	Gly	Leu	Glu	Asn	Met	Thr	Gln	Glu	Leu	Lys	His	Leu	Leu
1610						1615					1620			
Ser	Pro	Gln	Arg	Ala	Pro	Glu	Arg	Leu	Ile	Gln	Leu	Ala	Glu	Gly
1625						1630					1635			
Asn	Leu	Asn	Thr	Leu	Val	Thr	Glu	Met	Asn	Glu	Leu	Leu	Thr	Arg
1640						1645					1650			
Ala	Thr	Lys	Val	Thr	Ala	Asp	Gly	Glu	Gln	Thr	Gly	Gln	Asp	Ala
1655						1660					1665			
Glu	Arg	Thr	Asn	Thr	Arg	Ala	Lys	Ser	Leu	Gly	Glu	Phe	Ile	Lys
1670						1675					1680			
Glu	Leu	Ala	Arg	Asp	Ala	Glu	Ala	Val	Asn	Glu	Lys	Ala	Ile	Lys
1685						1690					1695			
Leu	Asn	Glu	Thr	Leu	Gly	Thr	Arg	Asp	Glu	Ala	Phe	Glu	Arg	Asn
1700						1705					1710			
Leu	Glu	Gly	Leu	Gln	Lys	Glu	Ile	Asp	Gln	Met	Ile	Lys	Glu	Leu
1715						1720					1725			
Arg	Arg	Lys	Asn	Leu	Glu	Thr	Gln	Lys	Glu	Ile	Ala	Glu	Asp	Glu
1730						1735					1740			
Leu	Val	Ala	Ala	Glu	Ala	Leu	Leu	Lys	Lys	Val	Lys	Lys	Leu	Phe
1745						1750					1755			
Gly	Glu	Ser	Arg	Gly	Glu	Asn	Glu	Glu	Met	Glu	Lys	Asp	Leu	Arg
1760						1765					1770			
Glu	Lys	Leu	Ala	Asp	Tyr	Lys	Asn	Lys	Val	Asp	Asp	Ala	Trp	Asp
1775						1780					1785			

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Leu	Leu	Arg	Glu	Ala	Thr	Asp	Lys	Ile	Arg	Glu	Ala	Asn	Arg	Leu
1790						1795					1800			
Phe	Ala	Val	Asn	Gln	Lys	Asn	Met	Thr	Ala	Leu	Glu	Lys	Lys	Lys
1805						1810					1815			
Glu	Ala	Val	Glu	Ser	Gly	Lys	Arg	Gln	Ile	Glu	Asn	Thr	Leu	Lys
1820						1825					1830			
Glu	Gly	Asn	Asp	Ile	Leu	Asp	Glu	Ala	Asn	Arg	Leu	Ala	Asp	Glu
1835						1840					1845			
Ile	Asn	Ser	Ile	Ile	Asp	Tyr	Val	Glu	Asp	Ile	Gln	Thr	Lys	Leu
1850						1855					1860			
Pro	Pro	Met	Ser	Glu	Glu	Leu	Asn	Asp	Lys	Ile	Asp	Asp	Leu	Ser
1865						1870					1875			
Gln	Glu	Ile	Lys	Asp	Arg	Lys	Leu	Ala	Glu	Lys	Val	Ser	Gln	Ala
1880						1885					1890			
Glu	Ser	His	Ala	Ala	Gln	Leu	Asn	Asp	Ser	Ser	Ala	Val	Leu	Asp
1895						1900					1905			
Gly	Ile	Leu	Asp	Glu	Ala	Lys	Asn	Ile	Ser	Phe	Asn	Ala	Thr	Ala
1910						1915					1920			
Ala	Phe	Lys	Ala	Tyr	Ser	Asn	Ile	Lys	Asp	Tyr	Ile	Asp	Glu	Ala
1925						1930					1935			
Glu	Lys	Val	Ala	Lys	Glu	Ala	Lys	Asp	Leu	Ala	His	Glu	Ala	Thr
1940						1945					1950			
Lys	Leu	Ala	Thr	Gly	Pro	Arg	Gly	Leu	Leu	Lys	Glu	Asp	Ala	Lys
1955						1960					1965			
Gly	Cys	Leu	Gln	Lys	Ser	Phe	Arg	Ile	Leu	Asn	Glu	Ala	Lys	Lys
1970						1975					1980			
Leu	Ala	Asn	Asp	Val	Lys	Glu	Asn	Glu	Asp	His	Leu	Asn	Gly	Leu
1985						1990					1995			
Lys	Thr	Arg	Ile	Glu	Asn	Ala	Asp	Ala	Arg	Asn	Gly	Asp	Leu	Leu
2000						2005					2010			
Arg	Thr	Leu	Asn	Asp	Thr	Leu	Gly	Lys	Leu	Ser	Ala	Ile	Pro	Asn
2015						2020					2025			
Asp	Thr	Ala	Ala	Lys	Leu	Gln	Ala	Val	Lys	Asp	Lys	Ala	Arg	Gln
2030						2035					2040			
Ala	Asn	Asp	Thr	Ala	Lys	Asp	Val	Leu	Ala	Gln	Ile	Thr	Glu	Leu
2045						2050					2055			
His	Gln	Asn	Leu	Asp	Gly	Leu	Lys	Lys	Asn	Tyr	Asn	Lys	Leu	Ala
2060						2065					2070			
Asp	Ser	Val	Ala	Lys	Thr	Asn	Ala	Val	Val	Lys	Asp	Pro	Ser	Lys
2075						2080					2085			

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Asn Lys	Ile Ile	Ala Asp	Ala Asp	Ala Thr	Val Lys	Asn Leu	Glu
2090			2095		2100		
Gln Glu	Ala Asp	Arg Leu	Ile Asp	Lys Leu	Lys Pro	Ile Lys	Glu
2105			2110		2115		
Leu Glu	Asp Asn	Leu Lys	Lys Asn	Ile Ser	Glu Ile	Lys Glu	Leu
2120			2125		2130		
Ile Asn	Gln Ala	Arg Lys	Gln Ala	Asn Ser	Ile Lys	Val Ser	Val
2135			2140		2145		
Ser Ser	Gly Gly	Asp Cys	Ile Arg	Thr Tyr	Lys Pro	Glu Ile	Lys
2150			2155		2160		
Lys Gly	Ser Tyr	Asn Asn	Ile Val	Val Asn	Val Lys	Thr Ala	Val
2165			2170		2175		
Ala Asp	Asn Leu	Leu Phe	Tyr Leu	Gly Ser	Ala Lys	Phe Ile	Asp
2180			2185		2190		
Phe Leu	Ala Ile	Glu Met	Arg Lys	Gly Lys	Val Ser	Phe Leu	Trp
2195			2200		2205		
Asp Val	Gly Ser	Gly Val	Gly Arg	Val Glu	Tyr Pro	Asp Leu	Thr
2210			2215		2220		
Ile Asp	Asp Ser	Tyr Trp	Tyr Arg	Ile Val	Ala Ser	Arg Thr	Gly
2225			2230		2235		
Arg Asn	Gly Thr	Ile Ser	Val Arg	Ala Leu	Asp Gly	Pro Lys	Ala
2240			2245		2250		
Ser Ile	Val Pro	Ser Thr	His His	Ser Thr	Ser Pro	Pro Gly	Tyr
2255			2260		2265		
Thr Ile	Leu Asp	Val Asp	Ala Asn	Ala Met	Leu Phe	Val Gly	Gly
2270			2275		2280		
Leu Thr	Gly Lys	Leu Lys	Lys Ala	Asp Ala	Val Arg	Val Ile	Thr
2285			2290		2295		
Phe Thr	Gly Cys	Met Gly	Glu Thr	Tyr Phe	Asp Asn	Lys Pro	Ile
2300			2305		2310		
Gly Leu	Trp Asn	Phe Arg	Glu Lys	Glu Gly	Asp Cys	Lys Gly	Cys
2315			2320		2325		
Thr Val	Ser Pro	Gln Val	Glu Asp	Ser Glu	Gly Thr	Ile Gln	Phe
2330			2335		2340		
Asp Gly	Glu Gly	Tyr Ala	Leu Val	Ser Arg	Pro Ile	Arg Trp	Tyr
2345			2350		2355		
Pro Asn	Ile Ser	Thr Val	Met Phe	Lys Phe	Arg Thr	Phe Ser	Ser
2360			2365		2370		
Ser Ala	Leu Leu	Met Tyr	Leu Ala	Thr Arg	Asp Leu	Arg Asp	Phe
2375			2380		2385		

Met	Ser	Val	Glu	Leu	Thr	Asp	Gly	His	Ile	Lys	Val	Ser	Tyr	Asp
2390						2395					2400			
Leu	Gly	Ser	Gly	Met	Ala	Ser	Val	Val	Ser	Asn	Gln	Asn	His	Asn
2405						2410					2415			
Asp	Gly	Lys	Trp	Lys	Ser	Phe	Thr	Leu	Ser	Arg	Ile	Gln	Lys	Gln
2420						2425					2430			
Ala	Asn	Ile	Ser	Ile	Val	Asp	Ile	Asp	Thr	Asn	Gln	Glu	Glu	Asn
2435						2440					2445			
Ile	Ala	Thr	Ser	Ser	Ser	Gly	Asn	Asn	Phe	Gly	Leu	Asp	Leu	Lys
2450						2455					2460			
Ala	Asp	Asp	Lys	Ile	Tyr	Phe	Gly	Gly	Leu	Pro	Thr	Leu	Arg	Asn
2465						2470					2475			
Leu	Ser	Met	Lys	Ala	Arg	Pro	Glu	Val	Asn	Leu	Lys	Lys	Tyr	Ser
2480						2485					2490			
Gly	Cys	Leu	Lys	Asp	Ile	Glu	Ile	Ser	Arg	Thr	Pro	Tyr	Asn	Ile
2495						2500					2505			
Leu	Ser	Ser	Pro	Asp	Tyr	Val	Gly	Val	Thr	Lys	Gly	Cys	Ser	Leu
2510						2515					2520			
Glu	Asn	Val	Tyr	Thr	Val	Ser	Phe	Pro	Lys	Pro	Gly	Phe	Val	Glu
2525						2530					2535			
Leu	Ser	Pro	Val	Pro	Ile	Asp	Val	Gly	Thr	Glu	Ile	Asn	Leu	Ser
2540						2545					2550			
Phe	Ser	Thr	Lys	Asn	Glu	Ser	Gly	Ile	Ile	Leu	Leu	Gly	Ser	Gly
2555						2560					2565			
Gly	Thr	Pro	Ala	Pro	Pro	Arg	Arg	Lys	Arg	Arg	Gln	Thr	Gly	Gln
2570						2575					2580			
Ala	Tyr	Tyr	Val	Ile	Leu	Leu	Asn	Arg	Gly	Arg	Leu	Glu	Val	His
2585						2590					2595			
Leu	Ser	Thr	Gly	Ala	Arg	Thr	Met	Arg	Lys	Ile	Val	Ile	Arg	Pro
2600						2605					2610			
Glu	Pro	Asn	Leu	Phe	His	Asp	Gly	Arg	Glu	His	Ser	Val	His	Val
2615						2620					2625			
Glu	Arg	Thr	Arg	Gly	Ile	Phe	Thr	Val	Gln	Val	Asp	Glu	Asn	Arg
2630						2635					2640			
Arg	Tyr	Met	Gln	Asn	Leu	Thr	Val	Glu	Gln	Pro	Ile	Glu	Val	Lys
2645						2650					2655			
Lys	Leu	Phe	Val	Gly	Gly	Ala	Pro	Pro	Glu	Phe	Gln	Pro	Ser	Pro
2660						2665					2670			
Leu	Arg	Asn	Ile	Pro	Pro	Phe	Glu	Gly	Cys	Ile	Trp	Asn	Leu	Val
2675						2680					2685			

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Ile	Asn	Ser	Val	Pro	Met	Asp	Phe	Ala	Arg	Pro	Val	Ser	Phe	Lys
2690						2695					2700			
Asn	Ala	Asp	Ile	Gly	Arg	Cys	Ala	His	Gln	Lys	Leu	Arg	Glu	Asp
2705						2710					2715			
Glu	Asp	Gly	Ala	Ala	Pro	Ala	Glu	Ile	Val	Ile	Gln	Pro	Glu	Pro
2720						2725					2730			
Val	Pro	Thr	Pro	Ala	Phe	Pro	Thr	Pro	Thr	Pro	Val	Leu	Thr	His
2735						2740					2745			
Gly	Pro	Cys	Ala	Ala	Glu	Ser	Glu	Pro	Ala	Leu	Leu	Ile	Gly	Ser
2750						2755					2760			
Lys	Gln	Phe	Gly	Leu	Ser	Arg	Asn	Ser	His	Ile	Ala	Ile	Ala	Phe
2765						2770					2775			
Asp	Asp	Thr	Lys	Val	Lys	Asn	Arg	Leu	Thr	Ile	Glu	Leu	Glu	Val
2780						2785					2790			
Arg	Thr	Glu	Ala	Glu	Ser	Gly	Leu	Leu	Phe	Tyr	Met	Ala	Ala	Ile
2795						2800					2805			
Asn	His	Ala	Asp	Phe	Ala	Thr	Val	Gln	Leu	Arg	Asn	Gly	Leu	Pro
2810						2815					2820			
Tyr	Phe	Ser	Tyr	Asp	Leu	Gly	Ser	Gly	Asp	Thr	His	Thr	Met	Ile
2825						2830					2835			
Pro	Thr	Lys	Ile	Asn	Asp	Gly	Gln	Trp	His	Lys	Ile	Lys	Ile	Met
2840						2845					2850			
Arg	Ser	Lys	Gln	Glu	Gly	Ile	Leu	Tyr	Val	Asp	Gly	Ala	Ser	Asn
2855						2860					2865			
Arg	Thr	Ile	Ser	Pro	Lys	Lys	Ala	Asp	Ile	Leu	Asp	Val	Val	Gly
2870						2875					2880			
Met	Leu	Tyr	Val	Gly	Gly	Leu	Pro	Ile	Asn	Tyr	Thr	Thr	Arg	Arg
2885						2890					2895			
Ile	Gly	Pro	Val	Thr	Tyr	Ser	Ile	Asp	Gly	Cys	Val	Arg	Asn	Leu
2900						2905					2910			
His	Met	Ala	Glu	Ala	Pro	Ala	Asp	Leu	Glu	Gln	Pro	Thr	Ser	Ser
2915						2920					2925			
Phe	His	Val	Gly	Thr	Cys	Phe	Ala	Asn	Ala	Gln	Arg	Gly	Thr	Tyr
2930						2935					2940			
Phe	Asp	Gly	Thr	Gly	Phe	Ala	Lys	Ala	Val	Gly	Gly	Phe	Lys	Val
2945						2950					2955			
Gly	Leu	Asp	Leu	Leu	Val	Glu	Phe	Glu	Phe	Ala	Thr	Thr	Thr	Thr
2960						2965					2970			
Thr	Gly	Val	Leu	Leu	Gly	Ile	Ser	Ser	Gln	Lys	Met	Asp	Gly	Met
2975						2980					2985			

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Gly Ile Glu Met Ile Asp Glu Lys Leu Met Phe His Val Asp Asn
 2990 2995 3000
 Gly Ala Gly Arg Phe Thr Ala Val Tyr Asp Ala Gly Val Pro Gly
 3005 3010 3015
 His Leu Cys Asp Gly Gln Trp His Lys Val Thr Ala Asn Lys Ile
 3020 3025 3030
 Lys His Arg Ile Glu Leu Thr Val Asp Gly Asn Gln Val Glu Ala
 3035 3040 3045
 Gln Ser Pro Asn Pro Ala Ser Thr Ser Ala Asp Thr Asn Asp Pro
 3050 3055 3060
 Val Phe Val Gly Gly Phe Pro Asp Asp Leu Lys Gln Phe Gly Leu
 3065 3070 3075
 Thr Thr Ser Ile Pro Phe Arg Gly Cys Ile Arg Ser Leu Lys Leu
 3080 3085 3090
 Thr Lys Gly Thr Ala Ser His Trp Arg Leu Ile Leu Pro Arg Pro
 3095 3100 3105
 Trp Asn
 3110
 <210> 87
 <211> 1798
 <212> PRT
 <213> Homo Sapiens
 <400> 87
 Met Glu Leu Thr Ser Thr Glu Arg Gly Arg Gly Gln Pro Leu Pro Trp
 1 5 10 15
 Glu Leu Arg Leu Pro Leu Leu Leu Ser Val Leu Ala Ala Thr Leu Ala
 20 25 30
 Gln Ala Pro Ala Pro Asp Val Pro Gly Cys Ser Arg Gly Ser Cys Tyr
 35 40 45
 Pro Ala Thr Ala Asp Leu Leu Val Gly Arg Ala Asp Arg Leu Thr Ala
 50 55 60
 Ser Ser Thr Cys Gly Leu Asn Gly Arg Gln Pro Tyr Cys Ile Val Ser
 65 70 75 80
 His Leu Gln Asp Glu Lys Lys Cys Phe Leu Cys Asp Ser Arg Arg Pro
 85 90 95
 Phe Ser Ala Arg Asp Asn Pro His Thr His Arg Ile Gln Asn Val Val
 100 105 110
 Thr Ser Phe Ala Pro Gln Arg Arg Ala Ala Trp Trp Gln Ser Gln Asn
 115 120 125
 Gly Ile Pro Ala Val Thr Ile Gln Leu Asp Leu Glu Ala Glu Phe His

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130	135	140
Phe Thr His Leu Ile Met Thr Phe Lys Thr Phe Arg Pro Ala Ala Met 145 150 155 160		
Leu Val Glu Arg Ser Ala Asp Phe Gly Arg Thr Trp His Val Tyr Arg 165 170 175		
Tyr Phe Ser Tyr His Cys Gly Ala Asp Phe Pro Gly Val Pro Leu Ala 180 185 190		
Pro Pro Arg His Trp Asp Asp Val Val Cys Glu Ser Arg Tyr Ser Glu 195 200 205		
Ile Glu Pro Ser Thr Glu Gly Glu Val Ile Tyr Arg Val Leu Asp Pro 210 215 220		
Ala Ile Pro Ile Pro Asp Pro Tyr Ser Ser Arg Ile Gln Asn Leu Leu 225 230 235 240		
Lys Ile Thr Asn Leu Arg Val Asn Leu Thr Arg Leu His Thr Leu Gly 245 250 255		
Asp Asn Leu Leu Asp Pro Arg Arg Glu Ile Arg Glu Lys Tyr Tyr Tyr 260 265 270		
Ala Leu Tyr Glu Leu Val Val Arg Gly Asn Cys Phe Cys Tyr Gly His 275 280 285		
Ala Ser Glu Cys Ala Pro Ala Pro Gly Ala Pro Ala His Ala Glu Gly 290 295 300		
Met Val His Gly Ala Cys Ile Cys Lys His Asn Thr Arg Gly Leu Asn 305 310 315 320		
Cys Glu Gln Cys Gln Asp Phe Tyr Arg Asp Leu Pro Trp Arg Pro Ala 325 330 335		
Glu Asp Gly His Ser His Ala Cys Arg Lys Cys Asp Arg His Gly His 340 345 350		
Thr His Ser Cys His Phe Asp Met Ala Val Tyr Leu Gly Ser Gly Asn 355 360 365		
Val Ser Gly Gly Val Cys Asp Gly Cys Gln His Asn Thr Ala Trp Arg 370 375 380		
His Cys Glu Leu Cys Arg Pro Phe Phe Tyr Arg Asp Pro Thr Lys Asp 385 390 395 400		
Leu Arg Asp Pro Ala Val Cys Arg Ser Cys Asp Cys Asp Pro Met Gly 405 410 415		
Ser Gln Asp Gly Gly Arg Cys Asp Ser His Asp Asp Pro Ala Leu Gly 420 425 430		
Leu Val Ser Gly Gln Cys Arg Cys Lys Glu His Val Val Gly Thr Arg 435 440 445		
Cys Gln Gln Cys Arg Asp Gly Phe Phe Gly Leu Ser Ile Ser Asp Pro		

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450		455		460	
Ser Gly Cys Arg Arg Cys Gln Cys Asn Ala Arg Gly Thr Val Pro Gly					
465		470		475	480
Ser Thr Pro Cys Asp Pro Asn Ser Gly Ser Cys Tyr Cys Lys Arg Leu					
	485		490		495
Val Thr Gly Arg Gly Cys Asp Arg Cys Leu Pro Gly His Trp Gly Leu					
	500		505		510
Ser Leu Asp Leu Leu Gly Cys Arg Pro Cys Asp Cys Asp Val Gly Gly					
	515		520		525
Ala Leu Asp Pro Gln Cys Asp Glu Gly Thr Gly Gln Cys His Cys Arg					
	530		535		540
Gln His Met Val Gly Arg Arg Cys Glu Gln Val Gln Pro Gly Tyr Phe					
	545		550		555
Arg Pro Phe Leu Asp His Leu Ile Trp Glu Ala Glu Asn Thr Arg Gly					
	565		570		575
Gln Val Leu Asp Val Val Glu Arg Leu Val Thr Pro Gly Glu Thr Pro					
	580		585		590
Ser Trp Thr Gly Ser Gly Phe Val Arg Leu Gln Glu Gly Gln Thr Leu					
	595		600		605
Glu Phe Leu Val Ala Ser Val Pro Asn Ala Met Asp Tyr Asp Leu Leu					
	610		615		620
Leu Arg Leu Glu Pro Gln Val Pro Glu Gln Trp Ala Glu Leu Glu Leu					
	625		630		635
Ile Val Gln Arg Pro Gly Pro Val Pro Ala His Ser Leu Cys Gly His					
	645		650		655
Leu Val Pro Arg Asp Asp Arg Ile Gln Gly Thr Leu Gln Pro His Ala					
	660		665		670
Arg Tyr Leu Ile Phe Pro Asn Pro Val Cys Leu Glu Pro Gly Ile Ser					
	675		680		685
Tyr Lys Leu His Leu Lys Leu Val Arg Thr Gly Gly Ser Ala Gln Pro					
	690		695		700
Glu Thr Pro Tyr Ser Gly Pro Gly Leu Leu Ile Asp Ser Leu Val Leu					
	705		710		715
Leu Pro Arg Val Leu Val Leu Glu Met Phe Ser Gly Gly Asp Ala Ala					
	725		730		735
Ala Leu Glu Arg Gln Ala Thr Phe Glu Arg Tyr Gln Cys His Glu Glu					
	740		745		750
Gly Leu Val Pro Ser Lys Thr Ser Pro Ser Glu Ala Cys Ala Pro Leu					
	755		760		765
Leu Ile Ser Leu Ser Thr Leu Ile Tyr Asn Gly Ala Leu Pro Cys Gln					

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770	775	780
Cys Asn Pro Gln Gly Ser Leu Ser Ser Glu Cys Asn Pro His Gly Gly		
785	790	795 800
Gln Cys Leu Cys Lys Pro Gly Val Val Gly Arg Arg Cys Asp Thr Cys		
	805	810 815
Ala Pro Gly Tyr Tyr Gly Phe Gly Pro Thr Gly Cys Gln Ala Cys Gln		
	820 825	830
Cys Ser Pro Arg Gly Ala Leu Ser Ser Leu Cys Glu Arg Thr Ser Gly		
	835 840	845
Gln Cys Leu Cys Arg Thr Gly Ala Phe Gly Leu Arg Cys Asp Ala Cys		
	850 855	860
Gln Arg Gly Gln Trp Gly Phe Pro Ser Cys Arg Pro Cys Val Cys Asn		
865	870 875	880
Gly His Ala Asp Glu Cys Asn Thr His Thr Gly Ala Cys Leu Gly Cys		
	885 890	895
Arg Asp Leu Thr Gly Gly Glu His Cys Glu Arg Cys Ile Ala Gly Phe		
	900 905	910
His Gly Asp Pro Arg Leu Pro Tyr Gly Ala Gln Cys Arg Pro Cys Pro		
	915 920	925
Cys Pro Glu Gly Pro Gly Ser Gln Arg His Phe Ala Thr Ser Cys His		
	930 935	940
Gln Asp Glu Tyr Ser Gln Gln Ile Val Cys His Cys Arg Ala Gly Tyr		
945	950 955	960
Thr Gly Leu Arg Cys Glu Ala Cys Ala Pro Gly Gln Phe Gly Asp Pro		
	965 970	975
Ser Arg Pro Gly Gly Arg Cys Gln Leu Cys Glu Cys Ser Gly Asn Ile		
	980 985	990
Asp Pro Met Asp Pro Asp Ala Cys Asp Pro His Pro Gly Gln Cys Leu		
	995 1000	1005
Arg Cys Leu His His Thr Glu Gly Pro His Cys Ala His Ser Lys		
	1010 1015	1020
Pro Gly Phe His Gly Gln Ala Ala Arg Gln Ser Cys His Arg Cys		
	1025 1030	1035
Thr Cys Asn Leu Leu Gly Thr Asn Pro Gln Gln Cys Pro Ser Pro		
	1040 1045	1050
Asp Gln Cys His Cys Asp Pro Ser Ser Gly Gln Cys Pro Cys Leu		
	1055 1060	1065
Pro Asn Val Gln Ala Leu Ala Val Asp Arg Cys Ala Pro Asn Phe		
	1070 1075	1080
Trp Asn Leu Thr Ser Gly His Gly Cys Gln Pro Cys Ala Cys Leu		

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1085		1090		1095
Pro Ser	Pro Glu Glu Gly	Pro Thr Cys Asn Glu	Phe Thr Gly Gln	
1100		1105	1110	
Cys His	Cys Leu Cys Gly	Phe Gly Gly Arg Thr	Cys Ser Glu Cys	
1115		1120	1125	
Gln Glu	Leu His Trp Gly	Asp Pro Gly Leu Gln	Cys His Ala Cys	
1130		1135	1140	
Asp Cys	Asp Ser Arg Gly	Ile Asp Thr Pro Gln	Cys His Arg Phe	
1145		1150	1155	
Thr Gly	His Cys Thr Cys	Arg Pro Gly Val Ser	Gly Val Arg Cys	
1160		1165	1170	
Asp Gln	Cys Ala Arg Gly	Phe Ser Gly Ile Phe	Pro Ala Cys His	
1175		1180	1185	
Pro Cys	His Ala Cys Phe	Gly Asp Trp Asp Arg	Val Val Gln Asp	
1190		1195	1200	
Leu Ala	Ala Arg Thr Gln	Arg Leu Glu Gln Arg	Ala Gln Glu Leu	
1205		1210	1215	
Gln Gln	Thr Gly Val Leu	Gly Ala Phe Glu Ser	Ser Phe Trp His	
1220		1225	1230	
Met Gln	Glu Lys Leu Gly	Ile Val Gln Gly Ile	Val Gly Ala Arg	
1235		1240	1245	
Asn Thr	Ser Ala Ala Ser	Thr Ala Gln Leu Val	Glu Ala Thr Glu	
1250		1255	1260	
Glu Leu	Arg Arg Glu Ile	Gly Glu Ala Thr Glu	His Leu Thr Gln	
1265		1270	1275	
Leu Glu	Ala Asp Leu Thr	Asp Val Gln Asp Glu	Asn Phe Asn Ala	
1280		1285	1290	
Asn His	Ala Leu Ser Gly	Leu Glu Arg Asp Arg	Leu Ala Leu Asn	
1295		1300	1305	
Leu Thr	Leu Arg Gln Leu	Asp Gln His Leu Asp	Leu Leu Lys His	
1310		1315	1320	
Ser Asn	Phe Leu Gly Ala	Tyr Asp Ser Ile Arg	His Ala His Ser	
1325		1330	1335	
Gln Ser	Ala Glu Ala Glu	Arg Arg Ala Asn Thr	Ser Ala Leu Ala	
1340		1345	1350	
Val Pro	Ser Pro Val Ser	Asn Ser Ala Ser Ala	Arg His Arg Thr	
1355		1360	1365	
Glu Ala	Leu Met Asp Ala	Gln Lys Glu Asp Phe	Asn Ser Lys His	
1370		1375	1380	
Met Ala	Asn Gln Arg Ala	Leu Gly Lys Leu Ser	Ala His Thr His	

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1385		1390		1395
Thr Leu Ser Leu Thr Asp	Ile Asn Glu Leu Val	Cys Gly Ala Gln		
1400	1405	1410		
Gly Leu His His Asp Arg	Thr Ser Pro Cys Gly	Gly Ala Gly Cys		
1415	1420	1425		
Arg Asp Glu Asp Gly Gln	Pro Arg Cys Gly Gly	Leu Ser Cys Asn		
1430	1435	1440		
Gly Ala Ala Ala Thr Ala	Asp Leu Ala Leu Gly	Arg Ala Arg His		
1445	1450	1455		
Thr Gln Ala Glu Leu Gln	Arg Ala Leu Ala Glu	Gly Gly Ser Ile		
1460	1465	1470		
Leu Ser Arg Val Ala Glu	Thr Arg Arg Gln Ala	Ser Glu Ala Gln		
1475	1480	1485		
Gln Arg Ala Gln Ala Ala	Leu Asp Lys Ala Asn	Ala Ser Arg Gly		
1490	1495	1500		
Gln Val Glu Gln Ala Asn	Gln Glu Leu Gln Glu	Leu Ile Gln Ser		
1505	1510	1515		
Val Lys Asp Phe Leu Asn	Gln Glu Gly Ala Asp	Pro Asp Ser Ile		
1520	1525	1530		
Glu Met Val Ala Thr Arg	Val Leu Glu Leu Ser	Ile Pro Ala Ser		
1535	1540	1545		
Ala Glu Gln Ile Gln His	Leu Ala Gly Ala Ile	Ala Glu Arg Val		
1550	1555	1560		
Arg Ser Leu Ala Asp Val	Asp Ala Ile Leu Ala	Arg Thr Val Gly		
1565	1570	1575		
Asp Val Arg Arg Ala Glu	Gln Leu Leu Gln Asp	Ala Arg Arg Ala		
1580	1585	1590		
Arg Ser Trp Ala Glu Asp	Glu Lys Gln Lys Ala	Glu Thr Val Gln		
1595	1600	1605		
Ala Ala Leu Glu Glu Ala	Gln Arg Ala Gln Gly	Ile Ala Gln Gly		
1610	1615	1620		
Ala Ile Arg Gly Ala Val	Ala Asp Thr Arg Asp	Thr Glu Gln Thr		
1625	1630	1635		
Leu Tyr Gln Val Gln Glu	Arg Met Ala Gly Ala	Glu Arg Ala Leu		
1640	1645	1650		
Ser Ser Ala Gly Glu Arg	Ala Arg Gln Leu Asp	Ala Leu Leu Glu		
1655	1660	1665		
Ala Leu Lys Leu Lys Arg	Ala Gly Asn Ser Leu	Ala Ala Ser Thr		
1670	1675	1680		
Ala Glu Glu Thr Ala Gly	Ser Ala Gln Gly Arg	Ala Gln Glu Ala		

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1685	1690	1695
Glu Gln Leu Leu Arg Gly Pro Leu Gly Asp Gln Tyr Gln Thr Val		
1700	1705	1710
Lys Ala Leu Ala Glu Arg Lys Ala Gln Gly Val Leu Ala Ala Gln		
1715	1720	1725
Ala Arg Ala Glu Gln Leu Pro Asp Glu Ala Arg Asp Leu Leu Gln		
1730	1735	1740
Ala Ala Gln Asp Lys Leu Gln Arg Leu Gln Glu Leu Glu Gly Thr		
1745	1750	1755
Tyr Glu Glu Asn Glu Arg Ala Leu Glu Ser Lys Ala Ala Gln Leu		
1760	1765	1770
Asp Gly Leu Glu Ala Arg Met Arg Ser Val Leu Gln Ala Ile Asn		
1775	1780	1785
Leu Gln Val Gln Ile Tyr Asn Thr Cys Gln		
1790	1795	

<210> 88
 <211> 615
 <212> PRT
 <213> Homo Sapiens

<400> 88

Met Pro Ser Arg Lys Phe Ala Asp Gly Glu Val Val Arg Gly Arg Trp
1 5 10 15
Pro Gly Ser Ser Leu Tyr Tyr Glu Val Glu Ile Leu Ser His Asp Ser
20 25 30
Thr Ser Gln Leu Tyr Thr Val Lys Tyr Lys Asp Gly Thr Glu Leu Glu
35 40 45
Leu Lys Glu Asn Asp Ile Lys Pro Leu Thr Ser Phe Arg Gln Arg Lys
50 55 60
Gly Gly Ser Thr Ser Ser Ser Pro Ser Arg Arg Arg Gly Ser Arg Ser
65 70 75 80
Arg Ser Arg Ser Arg Ser Pro Gly Arg Pro Pro Lys Ser Ala Arg Arg
85 90 95
Ser Ala Ser Ala Ser His Gln Ala Asp Ile Lys Glu Ala Arg Arg Glu
100 105 110
Val Glu Val Lys Leu Thr Pro Leu Ile Leu Lys Pro Phe Gly Asn Ser
115 120 125
Ile Ser Arg Tyr Asn Gly Glu Pro Glu His Ile Glu Arg Asn Asp Ala
130 135 140
Pro His Lys Asn Thr Gln Glu Lys Phe Ser Leu Ser Gln Glu Ser Ser
145 150 155 160

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Tyr Ile Ala Thr Gln Tyr Ser Leu Arg Pro Arg Arg Glu Glu Val Lys
 165 170 175
 Leu Lys Glu Ile Asp Ser Lys Glu Glu Lys Tyr Val Ala Lys Glu Leu
 180 185 190
 Ala Val Arg Thr Phe Glu Val Thr Pro Ile Arg Ala Lys Asp Leu Glu
 195 200 205
 Phe Gly Gly Val Pro Gly Val Phe Leu Ile Met Phe Gly Leu Pro Val
 210 215 220
 Phe Leu Phe Leu Leu Leu Leu Met Cys Lys Gln Lys Asp Pro Ser Leu
 225 230 235 240
 Leu Asn Phe Pro Pro Pro Leu Pro Ala Leu Tyr Glu Leu Trp Glu Thr
 245 250 255
 Arg Val Phe Gly Val Tyr Leu Leu Trp Phe Leu Ile Gln Val Leu Phe
 260 265 270
 Tyr Leu Leu Pro Ile Gly Lys Val Val Glu Gly Thr Pro Leu Ile Asp
 275 280 285
 Gly Arg Arg Leu Lys Tyr Arg Leu Asn Gly Phe Tyr Pro Phe Ile Leu
 290 295 300
 Thr Ser Ala Val Ile Gly Thr Ser Leu Phe Gln Gly Val Glu Phe His
 305 310 315 320
 Tyr Val Tyr Ser His Phe Leu Gln Phe Ala Leu Ala Ala Thr Val Phe
 325 330 335
 Cys Val Val Leu Ser Val Tyr Leu Tyr Met Arg Ser Leu Lys Ala Pro
 340 345 350
 Arg Asn Asp Leu Ser Pro Ala Ser Ser Gly Asn Ala Val Tyr Asp Phe
 355 360 365
 Phe Ile Gly Arg Glu Leu Asn Pro Arg Ile Gly Thr Phe Asp Leu Lys
 370 375 380
 Tyr Phe Cys Glu Leu Arg Pro Gly Leu Ile Gly Trp Val Val Ile Asn
 385 390 395 400
 Leu Val Met Leu Leu Ala Glu Met Lys Ile Gln Asp Arg Ala Val Pro
 405 410 415
 Ser Leu Ala Met Ile Leu Val Asn Ser Phe Gln Leu Leu Tyr Val Val
 420 425 430
 Asp Ala Leu Trp Asn Glu Glu Ala Leu Leu Thr Thr Met Asp Ile Ile
 435 440 445
 His Asp Gly Phe Gly Phe Met Leu Ala Phe Gly Asp Leu Val Trp Val
 450 455 460
 Pro Phe Ile Tyr Ser Phe Gln Ala Phe Tyr Leu Val Ser His Pro Asn
 465 470 475 480

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Glu Val Ser Trp Pro Met Ala Ser Leu Ile Ile Val Leu Lys Leu Cys
 485 490 495
 Gly Tyr Val Ile Phe Arg Gly Ala Asn Ser Gln Lys Asn Ala Phe Arg
 500 505 510
 Lys Asn Pro Ser Asp Pro Lys Leu Ala His Leu Lys Thr Ile His Thr
 515 520 525
 Ser Ser Gly Lys Asn Leu Leu Val Ser Gly Trp Trp Gly Phe Val Arg
 530 535 540
 His Pro Asn Tyr Leu Gly Asp Leu Ile Met Ala Leu Ala Trp Ser Leu
 545 550 555 560
 Pro Cys Gly Phe Asn His Ile Leu Pro Tyr Phe Tyr Ile Ile Tyr Phe
 565 570 575
 Thr Met Leu Leu Val His Arg Glu Ala Arg Asp Glu Tyr His Cys Lys
 580 585 590
 Lys Lys Tyr Gly Val Ala Trp Glu Lys Tyr Cys Gln Arg Val Pro Tyr
 595 600 605
 Arg Ile Phe Pro Tyr Ile Tyr
 610 615
 <210> 89
 <211> 660
 <212> PRT
 <213> Homo Sapiens
 <400> 89
 Met Glu Ala Leu Met Ala Arg Gly Ala Leu Thr Gly Pro Leu Arg Ala
 1 5 10 15
 Leu Cys Leu Leu Gly Cys Leu Leu Ser His Ala Ala Ala Ala Pro Ser
 20 25 30
 Pro Ile Ile Lys Phe Pro Gly Asp Val Ala Pro Lys Thr Asp Lys Glu
 35 40 45
 Leu Ala Val Gln Tyr Leu Asn Thr Phe Tyr Gly Cys Pro Lys Glu Ser
 50 55 60
 Cys Asn Leu Phe Val Leu Lys Asp Thr Leu Lys Lys Met Gln Lys Phe
 65 70 75 80
 Phe Gly Leu Pro Gln Thr Gly Asp Leu Asp Gln Asn Thr Ile Glu Thr
 85 90 95
 Met Arg Lys Pro Arg Cys Gly Asn Pro Asp Val Ala Asn Tyr Asn Phe
 100 105 110
 Phe Pro Arg Lys Pro Lys Trp Asp Lys Asn Gln Ile Thr Tyr Arg Ile
 115 120 125
 Ile Gly Tyr Thr Pro Asp Leu Asp Pro Glu Thr Val Asp Asp Ala Phe
 130 135 140

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Ala	Arg	Ala	Phe	Gln	Val	Trp	Ser	Asp	Val	Thr	Pro	Leu	Arg	Phe	Ser	145	150	155	160
Arg	Ile	His	Asp	Gly	Glu	Ala	Asp	Ile	Met	Ile	Asn	Phe	Gly	Arg	Trp	165	170	175	
Glu	His	Gly	Asp	Gly	Tyr	Pro	Phe	Asp	Gly	Lys	Asp	Gly	Leu	Leu	Ala	180	185	190	
His	Ala	Phe	Ala	Pro	Gly	Thr	Gly	Val	Gly	Gly	Asp	Ser	His	Phe	Asp	195	200	205	
Asp	Asp	Glu	Leu	Trp	Thr	Leu	Gly	Glu	Gly	Gln	Val	Val	Arg	Val	Lys	210	215	220	
Tyr	Gly	Asn	Ala	Asp	Gly	Glu	Tyr	Cys	Lys	Phe	Pro	Phe	Leu	Phe	Asn	225	230	235	240
Gly	Lys	Glu	Tyr	Asn	Ser	Cys	Thr	Asp	Thr	Gly	Arg	Ser	Asp	Gly	Phe	245	250	255	
Leu	Trp	Cys	Ser	Thr	Thr	Tyr	Asn	Phe	Glu	Lys	Asp	Gly	Lys	Tyr	Gly	260	265	270	
Phe	Cys	Pro	His	Glu	Ala	Leu	Phe	Thr	Met	Gly	Gly	Asn	Ala	Glu	Gly	275	280	285	
Gln	Pro	Cys	Lys	Phe	Pro	Phe	Arg	Phe	Gln	Gly	Thr	Ser	Tyr	Asp	Ser	290	295	300	
Cys	Thr	Thr	Glu	Gly	Arg	Thr	Asp	Gly	Tyr	Arg	Trp	Cys	Gly	Thr	Thr	305	310	315	320
Glu	Asp	Tyr	Asp	Arg	Asp	Lys	Lys	Tyr	Gly	Phe	Cys	Pro	Glu	Thr	Ala	325	330	335	
Met	Ser	Thr	Val	Gly	Gly	Asn	Ser	Glu	Gly	Ala	Pro	Cys	Val	Phe	Pro	340	345	350	
Phe	Thr	Phe	Leu	Gly	Asn	Lys	Tyr	Glu	Ser	Cys	Thr	Ser	Ala	Gly	Arg	355	360	365	
Ser	Asp	Gly	Lys	Met	Trp	Cys	Ala	Thr	Thr	Ala	Asn	Tyr	Asp	Asp	Asp	370	375	380	
Arg	Lys	Trp	Gly	Phe	Cys	Pro	Asp	Gln	Gly	Tyr	Ser	Leu	Phe	Leu	Val	385	390	395	400
Ala	Ala	His	Glu	Phe	Gly	His	Ala	Met	Gly	Leu	Glu	His	Ser	Gln	Asp	405	410	415	
Pro	Gly	Ala	Leu	Met	Ala	Pro	Ile	Tyr	Thr	Tyr	Thr	Lys	Asn	Phe	Arg	420	425	430	
Leu	Ser	Gln	Asp	Asp	Ile	Lys	Gly	Ile	Gln	Glu	Leu	Tyr	Gly	Ala	Ser	435	440	445	
Pro	Asp	Ile	Asp	Leu	Gly	Thr	Gly	Pro	Thr	Pro	Thr	Leu	Gly	Pro	Val	450	455	460	

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Thr Pro Glu Ile Cys Lys Gln Asp Ile Val Phe Asp Gly Ile Ala Gln
 465 470 475 480
 Ile Arg Gly Glu Ile Phe Phe Phe Lys Asp Arg Phe Ile Trp Arg Thr
 485 490 495
 Val Thr Pro Arg Asp Lys Pro Met Gly Pro Leu Leu Val Ala Thr Phe
 500 505 510
 Trp Pro Glu Leu Pro Glu Lys Ile Asp Ala Val Tyr Glu Ala Pro Gln
 515 520 525
 Glu Glu Lys Ala Val Phe Phe Ala Gly Asn Glu Tyr Trp Ile Tyr Ser
 530 535 540
 Ala Ser Thr Leu Glu Arg Gly Tyr Pro Lys Pro Leu Thr Ser Leu Gly
 545 550 555 560
 Leu Pro Pro Asp Val Gln Arg Val Asp Ala Ala Phe Asn Trp Ser Lys
 565 570 575
 Asn Lys Lys Thr Tyr Ile Phe Ala Gly Asp Lys Phe Trp Arg Tyr Asn
 580 585 590
 Glu Val Lys Lys Lys Met Asp Pro Gly Phe Pro Lys Leu Ile Ala Asp
 595 600 605
 Ala Trp Asn Ala Ile Pro Asp Asn Leu Asp Ala Val Val Asp Leu Gln
 610 615 620
 Gly Gly Gly His Ser Tyr Phe Phe Lys Gly Ala Tyr Tyr Leu Lys Leu
 625 630 635 640
 Glu Asn Gln Ser Leu Lys Ser Val Lys Phe Gly Ser Ile Lys Ser Asp
 645 650 655
 Trp Leu Gly Cys
 660

<210> 90
 <211> 430
 <212> PRT
 <213> Homo Sapiens

<400> 90

Leu Arg Tyr Gln Gln Leu Ile Lys Glu Asn Leu Lys Glu Ile Ala Lys
 1 5 10 15
 Leu Ile Thr Leu Glu Gln Gly Lys Thr Leu Ala Asp Ala Glu Gly Asp
 20 25 30
 Val Phe Arg Gly Leu Gln Val Val Glu His Ala Cys Ser Val Thr Ser
 35 40 45
 Leu Met Met Gly Glu Thr Met Pro Ser Ile Thr Lys Asp Met Asp Leu
 50 55 60
 Tyr Ser Tyr Arg Leu Pro Leu Gly Val Cys Ala Gly Ile Ala Pro Phe

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65					70					75					80
Asn	Phe	Pro	Ala	Met	Ile	Pro	Leu	Trp	Met	Phe	Pro	Met	Ala	Met	Val
				85					90					95	
Cys	Gly	Asn	Thr	Phe	Leu	Met	Lys	Pro	Ser	Glu	Arg	Val	Pro	Gly	Ala
			100					105					110		
Thr	Met	Leu	Leu	Ala	Lys	Leu	Leu	Gln	Asp	Ser	Gly	Ala	Pro	Asp	Gly
		115					120					125			
Thr	Leu	Asn	Ile	Ile	His	Gly	Gln	His	Glu	Ala	Val	Asn	Phe	Ile	Cys
	130					135					140				
Asp	His	Pro	Asp	Ile	Lys	Ala	Ile	Ser	Phe	Val	Gly	Ser	Asn	Lys	Ala
145					150					155					160
Gly	Glu	Tyr	Ile	Phe	Glu	Arg	Gly	Ser	Arg	His	Gly	Lys	Arg	Val	Gln
				165					170					175	
Ala	Asn	Met	Gly	Ala	Lys	Asn	His	Gly	Val	Val	Met	Pro	Asp	Ala	Asn
			180					185					190		
Lys	Glu	Asn	Thr	Leu	Asn	Gln	Leu	Val	Gly	Ala	Ala	Phe	Gly	Ala	Ala
		195					200					205			
Gly	Gln	Arg	Cys	Met	Ala	Leu	Ser	Thr	Ala	Val	Leu	Val	Gly	Glu	Ala
	210					215					220				
Lys	Lys	Trp	Leu	Pro	Glu	Leu	Val	Glu	His	Ala	Lys	Asn	Leu	Arg	Val
225					230					235					240
Asn	Ala	Gly	Asp	Gln	Pro	Gly	Ala	Asp	Leu	Gly	Pro	Leu	Ile	Thr	Pro
				245					250					255	
Gln	Ala	Lys	Glu	Arg	Val	Cys	Asn	Leu	Ile	Asp	Ser	Gly	Thr	Lys	Glu
			260					265					270		
Gly	Ala	Ser	Ile	Leu	Leu	Asp	Gly	Arg	Lys	Ile	Lys	Val	Lys	Gly	Tyr
		275					280					285			
Glu	Asn	Gly	Asn	Phe	Val	Gly	Pro	Thr	Ile	Ile	Ser	Asn	Val	Lys	Pro
	290					295					300				
Asn	Met	Thr	Cys	Tyr	Lys	Glu	Glu	Ile	Phe	Gly	Pro	Val	Leu	Val	Val
305					310					315					320
Leu	Glu	Thr	Glu	Thr	Leu	Asp	Glu	Ala	Ile	Gln	Ile	Val	Asn	Asn	Asn
			325						330				335		
Pro	Tyr	Gly	Asn	Gly	Thr	Ala	Ile	Phe	Thr	Thr	Asn	Gly	Ala	Thr	Ala
			340					345					350		
Arg	Lys	Tyr	Ala	His	Leu	Val	Asp	Val	Gly	Gln	Val	Gly	Val	Asn	Val
		355					360					365			
Pro	Ile	Pro	Val	Pro	Leu	Pro	Met	Phe	Ser	Phe	Thr	Gly	Ser	Arg	Ser
	370					375					380				
Ser	Phe	Arg	Gly	Asp	Thr	Asn	Phe	Tyr	Gly	Lys	Gln	Gly	Ile	Gln	Phe

385				390				395				400				
Tyr	Thr	Gln	Leu	Lys	Thr	Ile	Thr	Ser	Gln	Trp	Lys	Glu	Glu	Asp	Ala	
				405					410					415		
Thr	Leu	Ser	Ser	Pro	Ala	Val	Val	Met	Pro	Thr	Met	Gly	Arg			
				420					425					430		
<210> 91																
<211> 1857																
<212> PRT																
<213> Homo Sapiens																
<400> 91																
Thr	Tyr	Ser	Gly	Leu	Phe	Cys	Val	Val	Val	Asn	Pro	Tyr	Lys	His	Leu	
1					5					10					15	
Pro	Ile	Tyr	Ser	Glu	Lys	Ile	Val	Asp	Met	Tyr	Lys	Gly	Lys	Lys	Arg	
				20					25					30		
His	Glu	Met	Pro	Pro	His	Ile	Tyr	Ala	Ile	Ala	Asp	Thr	Ala	Tyr	Arg	
				35					40					45		
Ser	Met	Leu	Gln	Asp	Arg	Glu	Asp	Gln	Ser	Ile	Leu	Cys	Thr	Gly	Glu	
				50					55					60		
Ser	Gly	Ala	Gly	Lys	Thr	Glu	Asn	Thr	Lys	Lys	Val	Ile	Gln	Tyr	Leu	
65					70					75					80	
Ala	Val	Val	Ala	Ser	Ser	His	Lys	Gly	Lys	Lys	Asp	Thr	Ser	Ile	Thr	
				85					90					95		
Gly	Glu	Leu	Glu	Lys	Gln	Leu	Leu	Gln	Ala	Asn	Pro	Ile	Leu	Glu	Ala	
				100					105					110		
Phe	Gly	Asn	Ala	Lys	Thr	Val	Lys	Asn	Asp	Asn	Ser	Ser	Arg	Phe	Gly	
				115					120					125		
Lys	Phe	Ile	Arg	Ile	Asn	Phe	Asp	Val	Thr	Gly	Tyr	Ile	Val	Gly	Ala	
				130					135					140		
Asn	Ile	Glu	Thr	Tyr	Leu	Leu	Glu	Lys	Ser	Arg	Ala	Ile	Arg	Gln	Ala	
				145					150					155		
Arg	Asp	Glu	Arg	Thr	Phe	His	Ile	Phe	Tyr	Tyr	Met	Ile	Ala	Gly	Ala	
				165					170					175		
Lys	Glu	Lys	Met	Arg	Ser	Asp	Leu	Leu	Leu	Glu	Gly	Phe	Asn	Asn	Tyr	
				180					185					190		
Thr	Phe	Leu	Ser	Asn	Gly	Phe	Val	Pro	Ile	Pro	Ala	Ala	Gln	Asp	Asp	
				195					200					205		
Glu	Met	Phe	Gln	Glu	Thr	Val	Glu	Ala	Met	Ala	Ile	Met	Gly	Phe	Ser	
				210					215					220		
Glu	Glu	Glu	Gln	Leu	Ser	Ile	Leu	Lys	Val	Val	Ser	Ser	Val	Leu	Gln	
				225					230					235		

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Leu Gly Asn Ile Val Phe Lys Lys Glu Arg Asn Thr Asp Gln Ala Ser
 245 250 255
 Met Pro Asp Asn Thr Ala Ala Gln Lys Val Cys His Leu Met Gly Ile
 260 265 270
 Asn Val Thr Asp Phe Thr Arg Ser Ile Leu Thr Pro Arg Ile Lys Val
 275 280 285
 Gly Arg Asp Val Val Gln Lys Ala Gln Thr Lys Glu Gln Ala Asp Phe
 290 295 300
 Ala Val Glu Ala Leu Ala Lys Ala Thr Tyr Glu Arg Leu Phe Arg Trp
 305 310 315 320
 Ile Leu Thr Arg Val Asn Lys Ala Leu Asp Lys Thr His Arg Gln Gly
 325 330 335
 Ala Ser Phe Leu Gly Ile Leu Asp Ile Ala Gly Phe Glu Ile Phe Glu
 340 345 350
 Val Asn Ser Phe Glu Gln Leu Cys Ile Asn Tyr Thr Asn Glu Lys Leu
 355 360 365
 Gln Gln Leu Phe Asn His Thr Met Phe Ile Leu Glu Gln Glu Glu Tyr
 370 375 380
 Gln Arg Glu Gly Ile Glu Trp Asn Phe Ile Asp Phe Gly Leu Asp Leu
 385 390 395 400
 Gln Pro Cys Ile Glu Leu Ile Glu Arg Pro Asn Asn Pro Pro Gly Val
 405 410 415
 Leu Ala Leu Leu Asp Glu Glu Cys Trp Phe Pro Lys Ala Thr Asp Lys
 420 425 430
 Ser Phe Val Glu Lys Leu Cys Thr Glu Gln Gly Ser His Pro Lys Phe
 435 440 445
 Gln Lys Pro Lys Gln Leu Lys Asp Lys Thr Glu Phe Ser Ile Ile His
 450 455 460
 Tyr Ala Gly Lys Val Asp Tyr Asn Ala Ser Ala Trp Leu Thr Lys Asn
 465 470 475 480
 Met Asp Pro Leu Asn Asp Asn Val Thr Ser Leu Leu Asn Ala Ser Ser
 485 490 495
 Asp Lys Phe Val Ala Asp Leu Trp Lys Asp Val Asp Arg Ile Val Gly
 500 505 510
 Leu Asp Gln Met Ala Lys Met Thr Glu Ser Ser Leu Pro Ser Ala Ser
 515 520 525
 Lys Thr Lys Lys Gly Met Phe Arg Thr Val Gly Gln Leu Tyr Lys Glu
 530 535 540
 Gln Leu Gly Lys Leu Met Thr Thr Leu Arg Asn Thr Thr Pro Asn Phe
 545 550 555 560

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Val	Arg	Cys	Ile	Ile	Pro	Asn	His	Glu	Lys	Arg	Ser	Gly	Lys	Leu	Asp	565	570	575	
Ala	Phe	Leu	Val	Leu	Glu	Gln	Leu	Arg	Cys	Asn	Gly	Val	Leu	Glu	Gly	580	585	590	
Ile	Arg	Ile	Cys	Arg	Gln	Gly	Phe	Pro	Asn	Arg	Ile	Val	Phe	Gln	Glu	595	600	605	
Phe	Arg	Gln	Arg	Tyr	Glu	Ile	Leu	Ala	Ala	Asn	Ala	Ile	Pro	Lys	Gly	610	615	620	
Phe	Met	Asp	Gly	Lys	Gln	Ala	Cys	Ile	Leu	Met	Ile	Lys	Ala	Leu	Glu	625	630	635	640
Leu	Asp	Pro	Asn	Leu	Tyr	Arg	Ile	Gly	Gln	Ser	Lys	Ile	Phe	Phe	Arg	645	650	655	
Thr	Gly	Val	Leu	Ala	His	Leu	Glu	Glu	Glu	Arg	Asp	Leu	Lys	Ile	Thr	660	665	670	
Asp	Val	Ile	Met	Ala	Phe	Gln	Ala	Met	Cys	Arg	Gly	Tyr	Leu	Ala	Arg	675	680	685	
Lys	Ala	Phe	Ala	Lys	Arg	Gln	Gln	Gln	Leu	Thr	Ala	Met	Lys	Val	Ile	690	695	700	
Gln	Arg	Asn	Cys	Ala	Ala	Tyr	Leu	Lys	Leu	Arg	Asn	Trp	Gln	Trp	Trp	705	710	715	720
Arg	Leu	Phe	Thr	Lys	Val	Lys	Pro	Leu	Leu	Gln	Val	Thr	Arg	Gln	Glu	725	730	735	
Glu	Glu	Met	Gln	Ala	Lys	Glu	Asp	Glu	Leu	Gln	Lys	Thr	Lys	Glu	Arg	740	745	750	
Gln	Gln	Lys	Ala	Glu	Asn	Glu	Leu	Lys	Glu	Leu	Glu	Gln	Lys	His	Ser	755	760	765	
Gln	Leu	Thr	Glu	Glu	Lys	Asn	Leu	Leu	Gln	Glu	Gln	Leu	Gln	Ala	Glu	770	775	780	
Thr	Glu	Leu	Tyr	Ala	Glu	Ala	Glu	Glu	Met	Arg	Val	Arg	Leu	Ala	Ala	785	790	795	800
Lys	Lys	Gln	Glu	Leu	Glu	Glu	Ile	Leu	His	Glu	Met	Glu	Ala	Arg	Leu	805	810	815	
Glu	Glu	Glu	Glu	Asp	Arg	Gly	Gln	Gln	Leu	Gln	Ala	Glu	Arg	Lys	Lys	820	825	830	
Met	Ala	Gln	Gln	Met	Leu	Asp	Leu	Glu	Glu	Gln	Leu	Glu	Glu	Glu	Glu	835	840	845	
Ala	Ala	Arg	Gln	Lys	Leu	Gln	Leu	Glu	Lys	Val	Thr	Ala	Glu	Ala	Lys	850	855	860	
Ile	Lys	Lys	Leu	Glu	Asp	Glu	Ile	Leu	Val	Met	Asp	Asp	Gln	Asn	Asn	865	870	875	880

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Lys Leu Ser Lys Glu Arg Lys Leu Leu Glu Glu Arg Ile Ser Asp Leu
 885 890 895
 Thr Thr Asn Leu Ala Glu Glu Glu Glu Lys Ala Lys Asn Leu Thr Lys
 900 905 910
 Leu Lys Asn Lys His Glu Ser Met Ile Ser Glu Leu Glu Val Arg Leu
 915 920 925
 Lys Lys Glu Glu Lys Ser Arg Gln Glu Leu Glu Lys Leu Lys Arg Lys
 930 935 940
 Leu Glu Gly Asp Ala Ser Asp Phe His Glu Gln Ile Ala Asp Leu Gln
 945 950 955 960
 Ala Gln Ile Ala Glu Leu Lys Met Gln Leu Ala Lys Lys Glu Glu Glu
 965 970 975
 Leu Gln Ala Ala Leu Ala Arg Leu Asp Asp Glu Ile Ala Gln Lys Asn
 980 985 990
 Asn Ala Leu Lys Lys Ile Arg Glu Leu Glu Gly His Ile Ser Asp Leu
 995 1000 1005
 Gln Glu Asp Leu Asp Ser Glu Arg Ala Ala Arg Asn Lys Ala Glu
 1010 1015 1020
 Lys Gln Lys Arg Asp Leu Gly Glu Glu Leu Glu Ala Leu Lys Thr
 1025 1030 1035
 Glu Leu Glu Asp Thr Leu Asp Ser Thr Ala Thr Gln Gln Glu Leu
 1040 1045 1050
 Arg Ala Lys Arg Glu Gln Glu Val Thr Val Leu Lys Lys Ala Leu
 1055 1060 1065
 Asp Glu Glu Thr Arg Ser His Glu Ala Gln Val Gln Glu Met Arg
 1070 1075 1080
 Gln Lys His Ala Gln Ala Val Glu Glu Leu Thr Glu Gln Leu Glu
 1085 1090 1095
 Gln Phe Lys Arg Ala Lys Ala Asn Leu Asp Lys Asn Lys Gln Thr
 1100 1105 1110
 Leu Glu Lys Glu Asn Ala Asp Leu Ala Gly Glu Leu Arg Val Leu
 1115 1120 1125
 Gly Gln Ala Lys Gln Glu Val Glu His Lys Lys Lys Lys Leu Glu
 1130 1135 1140
 Ala Gln Val Gln Glu Leu Gln Ser Lys Cys Ser Asp Gly Glu Arg
 1145 1150 1155
 Ala Arg Ala Glu Leu Asn Asp Lys Val His Lys Leu Gln Asn Glu
 1160 1165 1170
 Val Glu Ser Val Thr Gly Met Leu Asn Glu Ala Glu Gly Lys Ala
 1175 1180 1185

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Glu	Leu	Glu	Asp	Glu	Arg	Lys	Gln	Arg	Ala	Leu	Ala	Ala	Ala	Ala
	1490					1495					1500			
Lys	Lys	Lys	Leu	Glu	Gly	Asp	Leu	Lys	Asp	Leu	Glu	Leu	Gln	Ala
	1505					1510					1515			
Asp	Ser	Ala	Ile	Lys	Gly	Arg	Glu	Glu	Ala	Ile	Lys	Gln	Leu	Arg
	1520					1525					1530			
Lys	Leu	Gln	Ala	Gln	Met	Lys	Asp	Phe	Gln	Arg	Glu	Leu	Glu	Asp
	1535					1540					1545			
Ala	Arg	Ala	Ser	Arg	Asp	Glu	Ile	Phe	Ala	Thr	Ala	Lys	Glu	Asn
	1550					1555					1560			
Glu	Lys	Lys	Ala	Lys	Ser	Leu	Glu	Ala	Asp	Leu	Met	Gln	Leu	Gln
	1565					1570					1575			
Glu	Asp	Leu	Ala	Ala	Ala	Glu	Arg	Ala	Arg	Lys	Gln	Ala	Asp	Leu
	1580					1585					1590			
Glu	Lys	Glu	Glu	Leu	Ala	Glu	Glu	Leu	Ala	Ser	Ser	Leu	Ser	Gly
	1595					1600					1605			
Arg	Asn	Ala	Leu	Gln	Asp	Glu	Lys	Arg	Arg	Leu	Glu	Ala	Arg	Ile
	1610					1615					1620			
Ala	Gln	Leu	Glu	Glu	Glu	Leu	Glu	Glu	Glu	Gln	Gly	Asn	Met	Glu
	1625					1630					1635			
Ala	Met	Ser	Asp	Arg	Val	Arg	Lys	Ala	Thr	Gln	Gln	Ala	Glu	Gln
	1640					1645					1650			
Leu	Ser	Asn	Glu	Leu	Ala	Thr	Glu	Arg	Ser	Thr	Ala	Gln	Lys	Asn
	1655					1660					1665			
Glu	Ser	Ala	Arg	Gln	Gln	Leu	Glu	Arg	Gln	Asn	Lys	Glu	Leu	Arg
	1670					1675					1680			
Ser	Lys	Leu	His	Glu	Met	Glu	Gly	Ala	Val	Lys	Ser	Lys	Phe	Lys
	1685					1690					1695			
Ser	Thr	Ile	Ala	Ala	Leu	Glu	Ala	Lys	Ile	Ala	Gln	Leu	Glu	Glu
	1700					1705					1710			
Gln	Val	Glu	Gln	Glu	Ala	Arg	Glu	Lys	Gln	Ala	Ala	Thr	Lys	Ser
	1715					1720					1725			
Leu	Lys	Gln	Lys	Asp	Lys	Lys	Leu	Lys	Glu	Ile	Leu	Leu	Gln	Val
	1730					1735					1740			
Glu	Asp	Glu	Arg	Lys	Met	Ala	Glu	Gln	Tyr	Lys	Glu	Gln	Ala	Glu
	1745					1750					1755			
Lys	Gly	Asn	Ala	Arg	Val	Lys	Gln	Leu	Lys	Arg	Gln	Leu	Glu	Glu
	1760					1765					1770			
Ala	Glu	Glu	Glu	Ser	Gln	Arg	Ile	Asn	Ala	Asn	Arg	Arg	Lys	Leu
	1775					1780					1785			

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Gln Arg Glu Leu Asp Glu Ala Thr Glu Ser Asn Glu Ala Met Gly
 1790 1795 1800
 Arg Glu Val Asn Ala Leu Lys Ser Lys Leu Arg Arg Gly Asn Glu
 1805 1810 1815
 Thr Ser Phe Val Pro Ser Arg Arg Ser Gly Gly Arg Arg Val Ile
 1820 1825 1830
 Glu Asn Ala Asp Gly Ser Glu Glu Glu Thr Asp Thr Arg Asp Ala
 1835 1840 1845
 Asp Phe Asn Gly Thr Lys Ala Ser Glu
 1850 1855
 <210> 92
 <211> 1953
 <212> PRT
 <213> Homo Sapiens
 <400> 92
 Gly Cys Leu Cys Cys Ser Ser Glu Gln Leu Gln Glu Leu Pro Ser Arg
 1 5 10 15
 Glu Leu Gln Asp Ala Phe Pro Val Pro Leu Ala Gln Leu Pro Gln Gln
 20 25 30
 Thr Thr Glu Lys Thr Val Thr Met Gly Asp Val Lys Leu Val Ala Ser
 35 40 45
 Ser His Ile Ser Lys Thr Ser Leu Ser Val Asp Pro Ser Arg Val Asp
 50 55 60
 Ser Met Pro Leu Thr Glu Ala Pro Ala Phe Ile Leu Pro Pro Arg Asn
 65 70 75 80
 Leu Cys Ile Lys Glu Gly Ala Thr Ala Lys Phe Glu Gly Arg Val Arg
 85 90 95
 Gly Tyr Pro Glu Pro Gln Val Thr Trp His Arg Asn Gly Gln Pro Ile
 100 105 110
 Thr Ser Gly Gly Arg Phe Leu Leu Asp Cys Gly Ile Arg Gly Thr Phe
 115 120 125
 Ser Leu Val Ile His Ala Val His Glu Glu Asp Arg Gly Lys Tyr Thr
 130 135 140
 Cys Glu Ala Thr Asn Gly Ser Gly Ala Arg Gln Val Thr Val Glu Leu
 145 150 155 160
 Thr Val Glu Gly Ser Phe Ala Lys Gln Leu Gly Gln Pro Val Val Ser
 165 170 175
 Lys Thr Leu Gly Asp Arg Phe Ser Ala Ser Ala Val Glu Thr Arg Pro
 180 185 190
 Ser Ile Trp Gly Glu Cys Pro Pro Lys Phe Ala Thr Lys Leu Gly Arg
 195 200 205

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Val	Val	Val	Lys	Glu	Gly	Gln	Met	Gly	Arg	Phe	Ser	Cys	Lys	Ile	Thr
210						215					220				
Gly	Arg	Pro	Gln	Pro	Gln	Val	Thr	Trp	Leu	Lys	Gly	Asn	Val	Pro	Leu
225					230					235					240
Gln	Pro	Ser	Ala	Arg	Val	Ser	Val	Ser	Glu	Lys	Asn	Gly	Met	Gln	Val
				245					250					255	
Leu	Glu	Ile	His	Gly	Val	Asn	Gln	Asp	Asp	Val	Gly	Val	Tyr	Thr	Cys
			260					265					270		
Leu	Val	Val	Asn	Gly	Ser	Gly	Lys	Ala	Ser	Met	Ser	Ala	Glu	Leu	Ser
		275					280					285			
Ile	Gln	Gly	Leu	Asp	Ser	Ala	Asn	Arg	Ser	Phe	Val	Arg	Glu	Thr	Lys
290						295					300				
Ala	Thr	Asn	Ser	Asp	Val	Arg	Lys	Glu	Val	Thr	Asn	Val	Ile	Ser	Lys
305					310					315					320
Glu	Ser	Lys	Leu	Asp	Ser	Leu	Glu	Ala	Ala	Ala	Lys	Ser	Lys	Asn	Cys
				325				330						335	
Ser	Ser	Pro	Gln	Arg	Gly	Gly	Ser	Pro	Pro	Trp	Ala	Ala	Asn	Ser	Gln
			340					345					350		
Pro	Gln	Pro	Pro	Arg	Glu	Ser	Lys	Leu	Glu	Ser	Cys	Lys	Asp	Ser	Pro
		355					360					365			
Arg	Thr	Ala	Pro	Gln	Thr	Pro	Val	Leu	Gln	Lys	Thr	Ser	Ser	Ser	Ile
	370					375					380				
Thr	Leu	Gln	Ala	Ala	Arg	Val	Gln	Pro	Glu	Pro	Arg	Ala	Pro	Gly	Leu
385					390					395					400
Gly	Val	Leu	Ser	Pro	Ser	Gly	Glu	Glu	Arg	Lys	Arg	Pro	Ala	Pro	Pro
				405					410					415	
Arg	Pro	Ala	Thr	Phe	Pro	Thr	Arg	Gln	Pro	Gly	Leu	Gly	Ser	Gln	Asp
			420					425					430		
Val	Val	Ser	Lys	Ala	Ala	Asn	Arg	Arg	Ile	Pro	Met	Glu	Gly	Gln	Arg
		435					440					445			
Asp	Ser	Ala	Phe	Pro	Lys	Phe	Glu	Ser	Lys	Pro	Gln	Ser	Gln	Glu	Val
	450					455					460				
Lys	Glu	Asn	Gln	Thr	Val	Lys	Phe	Arg	Cys	Glu	Val	Ser	Gly	Ile	Pro
465					470					475					480
Lys	Pro	Glu	Val	Ala	Trp	Phe	Leu	Glu	Gly	Thr	Pro	Val	Arg	Arg	Gln
				485					490					495	
Glu	Gly	Ser	Ile	Glu	Val	Tyr	Glu	Asp	Ala	Gly	Ser	His	Tyr	Leu	Cys
			500					505					510		
Leu	Leu	Lys	Ala	Arg	Thr	Arg	Asp	Ser	Gly	Thr	Tyr	Ser	Cys	Thr	Ala
		515					520					525			

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Ser	Asn	Ala	Gln	Gly	Gln	Val	Ser	Cys	Ser	Trp	Thr	Leu	Gln	Val	Glu
530						535					540				
Arg	Leu	Ala	Val	Met	Glu	Val	Ala	Pro	Ser	Phe	Ser	Ser	Val	Leu	Lys
545					550					555					560
Asp	Cys	Ala	Val	Ile	Glu	Gly	Gln	Asp	Phe	Val	Leu	Gln	Cys	Ser	Val
				565					570					575	
Arg	Gly	Thr	Pro	Val	Pro	Arg	Ile	Thr	Trp	Leu	Leu	Asn	Gly	Gln	Pro
			580					585					590		
Ile	Gln	Tyr	Ala	Arg	Ser	Thr	Cys	Glu	Ala	Gly	Val	Ala	Glu	Leu	His
		595					600					605			
Ile	Gln	Asp	Ala	Leu	Pro	Glu	Asp	His	Gly	Thr	Tyr	Thr	Cys	Leu	Ala
	610					615					620				
Glu	Asn	Ala	Leu	Gly	Gln	Val	Ser	Cys	Ser	Ala	Trp	Val	Thr	Val	His
625					630					635					640
Glu	Lys	Lys	Ser	Ser	Arg	Lys	Ser	Glu	Tyr	Leu	Leu	Pro	Val	Ala	Pro
				645					650					655	
Ser	Lys	Pro	Thr	Ala	Pro	Ile	Phe	Leu	Gln	Gly	Leu	Ser	Asp	Leu	Lys
			660					665					670		
Val	Met	Asp	Gly	Ser	Gln	Val	Thr	Met	Thr	Val	Gln	Val	Ser	Gly	Asn
		675					680					685			
Pro	Pro	Pro	Glu	Val	Ile	Trp	Leu	His	Asn	Gly	Asn	Glu	Ile	Gln	Glu
	690					695					700				
Ser	Glu	Asp	Phe	His	Phe	Glu	Gln	Arg	Gly	Thr	Gln	His	Ser	Leu	Trp
705					710					715					720
Ile	Gln	Glu	Val	Phe	Pro	Glu	Asp	Thr	Gly	Thr	Tyr	Thr	Cys	Glu	Ala
				725					730					735	
Trp	Asn	Ser	Ala	Gly	Glu	Val	Arg	Thr	Gln	Ala	Val	Leu	Thr	Val	Gln
			740					745					750		
Glu	Pro	His	Asp	Gly	Thr	Gln	Pro	Trp	Phe	Ile	Ser	Lys	Pro	Arg	Ser
		755					760					765			
Val	Thr	Ala	Ser	Leu	Gly	Gln	Ser	Val	Leu	Ile	Ser	Cys	Ala	Ile	Ala
	770					775					780				
Gly	Asp	Pro	Phe	Pro	Thr	Val	His	Trp	Leu	Arg	Asp	Gly	Lys	Ala	Leu
785					790					795					800
Cys	Lys	Asp	Thr	Gly	His	Phe	Glu	Val	Leu	Gln	Asn	Glu	Asp	Val	Phe
				805					810					815	
Thr	Leu	Val	Leu	Lys	Lys	Val	Gln	Pro	Trp	His	Ala	Gly	Gln	Tyr	Glu
			820					825					830		
Ile	Leu	Leu	Lys	Asn	Arg	Val	Gly	Glu	Cys	Ser	Cys	Gln	Val	Ser	Leu
		835					840					845			

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Met Leu Gln Asn Ser Ser Ala Arg Ala Leu Pro Arg Gly Arg Glu Pro
 850 855 860

Ala Ser Cys Glu Asp Leu Cys Gly Gly Gly Val Gly Ala Asp Gly Gly
 865 870 875 880

Gly Ser Asp Arg Tyr Gly Ser Leu Arg Pro Gly Trp Pro Ala Arg Gly
 885 890 895

Gln Gly Trp Leu Glu Glu Glu Asp Gly Glu Asp Val Arg Gly Val Leu
 900 905 910

Lys Arg Arg Val Glu Thr Arg Gln His Thr Glu Glu Ala Ile Arg Gln
 915 920 925

Gln Glu Val Glu Gln Leu Asp Phe Arg Asp Leu Leu Gly Lys Lys Val
 930 935 940

Ser Thr Lys Thr Leu Ser Glu Asp Asp Leu Lys Glu Ile Pro Ala Glu
 945 950 955 960

Gln Met Asp Phe Arg Ala Asn Leu Gln Arg Gln Val Lys Pro Lys Thr
 965 970 975

Val Ser Glu Glu Glu Arg Lys Val His Ser Pro Gln Gln Val Asp Phe
 980 985 990

Arg Ser Val Leu Ala Lys Lys Gly Thr Ser Lys Thr Pro Val Pro Glu
 995 1000 1005

Lys Val Pro Pro Pro Lys Pro Ala Thr Pro Asp Phe Arg Ser Val
 1010 1015 1020

Leu Gly Gly Lys Lys Lys Leu Pro Ala Glu Asn Gly Ser Ser Ser
 1025 1030 1035

Ala Glu Thr Leu Asn Ala Lys Ala Val Glu Ser Ser Lys Pro Leu
 1040 1045 1050

Ser Asn Ala Gln Pro Ser Gly Pro Leu Lys Pro Val Gly Asn Ala
 1055 1060 1065

Lys Pro Ala Glu Thr Leu Lys Pro Met Gly Asn Ala Lys Pro Ala
 1070 1075 1080

Glu Thr Leu Lys Pro Met Gly Asn Ala Lys Pro Asp Glu Asn Leu
 1085 1090 1095

Lys Ser Ala Ser Lys Glu Glu Leu Lys Lys Asp Val Lys Asn Asp
 1100 1105 1110

Val Asn Cys Lys Arg Gly His Ala Gly Thr Thr Asp Asn Glu Lys
 1115 1120 1125

Arg Ser Glu Ser Gln Gly Thr Ala Pro Ala Phe Lys Gln Lys Leu
 1130 1135 1140

Gln Asp Val His Val Ala Glu Gly Lys Lys Leu Leu Leu Gln Cys
 1145 1150 1155

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Gln Val	Ser Ser Asp Pro	Pro	Ala Thr Ile Ile	Trp	Thr Leu Asn
1160		1165		1170	
Gly Lys	Thr Leu Lys Thr	Thr	Lys Phe Ile Ile	Leu	Ser Gln Glu
1175		1180		1185	
Gly Ser	Leu Cys Ser Val	Ser	Ile Glu Lys Ala	Leu	Pro Glu Asp
1190		1195		1200	
Arg Gly	Leu Tyr Lys Cys	Val	Ala Lys Asn Asp	Ala	Gly Gln Ala
1205		1210		1215	
Glu Cys	Ser Cys Gln Val	Thr	Val Asp Asp Ala	Pro	Ala Ser Glu
1220		1225		1230	
Asn Thr	Lys Ala Pro Glu	Met	Lys Ser Arg Arg	Pro	Lys Ser Ser
1235		1240		1245	
Leu Pro	Pro Val Leu Gly	Thr	Glu Ser Asp Ala	Thr	Val Lys Lys
1250		1255		1260	
Lys Pro	Ala Pro Lys Thr	Pro	Pro Lys Ala Ala	Met	Pro Pro Gln
1265		1270		1275	
Ile Ile	Gln Phe Pro Glu	Asp	Gln Lys Val Arg	Ala	Gly Glu Ser
1280		1285		1290	
Val Glu	Leu Phe Gly Lys	Val	Thr Gly Thr Gln	Pro	Ile Thr Cys
1295		1300		1305	
Thr Trp	Met Lys Phe Arg	Lys	Gln Ile Gln Glu	Ser	Glu His Met
1310		1315		1320	
Lys Val	Glu Asn Ser Glu	Asn	Gly Ser Lys Leu	Thr	Ile Leu Ala
1325		1330		1335	
Ala Arg	Gln Glu His Cys	Gly	Cys Tyr Thr Leu	Leu	Val Glu Asn
1340		1345		1350	
Lys Leu	Gly Ser Arg Gln	Ala	Gln Val Asn Leu	Thr	Val Val Asp
1355		1360		1365	
Lys Pro	Asp Pro Pro Ala	Gly	Thr Pro Cys Ala	Ser	Asp Ile Arg
1370		1375		1380	
Ser Ser	Ser Leu Thr Leu	Ser	Trp Tyr Gly Ser	Ser	Tyr Asp Gly
1385		1390		1395	
Gly Ser	Ala Val Gln Ser	Tyr	Ser Ile Glu Ile	Trp	Asp Ser Ala
1400		1405		1410	
Asn Lys	Thr Trp Lys Glu	Leu	Ala Thr Cys Arg	Ser	Thr Ser Phe
1415		1420		1425	
Asn Val	Gln Asp Leu Leu	Pro	Asp His Glu Tyr	Lys	Phe Arg Val
1430		1435		1440	
Arg Ala	Ile Asn Val Tyr	Gly	Thr Ser Glu Pro	Ser	Gln Glu Ser
1445		1450		1455	

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Glu	Leu	Thr	Thr	Val	Gly	Glu	Lys	Pro	Glu	Glu	Pro	Lys	Asp	Glu
1460						1465					1470			
Val	Glu	Val	Ser	Asp	Asp	Asp	Glu	Lys	Glu	Pro	Glu	Val	Asp	Tyr
1475						1480					1485			
Arg	Thr	Val	Thr	Ile	Asn	Thr	Glu	Gln	Lys	Val	Ser	Asp	Phe	Tyr
1490						1495					1500			
Asp	Ile	Glu	Glu	Arg	Leu	Gly	Ser	Gly	Lys	Phe	Gly	Gln	Val	Phe
1505						1510					1515			
Arg	Leu	Val	Glu	Lys	Lys	Thr	Arg	Lys	Val	Trp	Ala	Gly	Lys	Phe
1520						1525					1530			
Phe	Lys	Ala	Tyr	Ser	Ala	Lys	Glu	Lys	Glu	Asn	Ile	Arg	Gln	Glu
1535						1540					1545			
Ile	Ser	Ile	Met	Asn	Cys	Leu	His	His	Pro	Lys	Leu	Val	Gln	Cys
1550						1555					1560			
Val	Asp	Ala	Phe	Glu	Glu	Lys	Ala	Asn	Ile	Val	Met	Val	Leu	Glu
1565						1570					1575			
Ile	Val	Ser	Gly	Gly	Glu	Leu	Phe	Glu	Arg	Ile	Ile	Asp	Glu	Asp
1580						1585					1590			
Phe	Glu	Leu	Thr	Glu	Arg	Glu	Cys	Ile	Lys	Tyr	Met	Arg	Gln	Ile
1595						1600					1605			
Ser	Glu	Gly	Val	Glu	Tyr	Ile	His	Lys	Gln	Gly	Ile	Val	His	Leu
1610						1615					1620			
Asp	Leu	Lys	Pro	Glu	Asn	Ile	Met	Cys	Val	Asn	Lys	Thr	Gly	Thr
1625						1630					1635			
Arg	Ile	Lys	Leu	Ile	Asp	Phe	Gly	Leu	Ala	Arg	Arg	Leu	Glu	Asn
1640						1645					1650			
Ala	Gly	Ser	Leu	Lys	Val	Leu	Phe	Gly	Thr	Pro	Glu	Phe	Val	Ala
1655						1660					1665			
Pro	Glu	Val	Ile	Asn	Tyr	Glu	Pro	Ile	Gly	Tyr	Ala	Thr	Asp	Met
1670						1675					1680			
Trp	Ser	Ile	Gly	Val	Ile	Cys	Tyr	Ile	Leu	Val	Ser	Gly	Leu	Ser
1685						1690					1695			
Pro	Phe	Met	Gly	Asp	Asn	Asp	Asn	Glu	Thr	Leu	Ala	Asn	Val	Thr
1700						1705					1710			
Ser	Ala	Thr	Trp	Asp	Phe	Asp	Asp	Glu	Ala	Phe	Asp	Glu	Ile	Ser
1715						1720					1725			
Asp	Asp	Ala	Lys	Asp	Phe	Ile	Ser	Asn	Leu	Leu	Lys	Lys	Asp	Met
1730						1735					1740			
Lys	Asn	Arg	Leu	Asp	Cys	Thr	Gln	Cys	Leu	Gln	His	Pro	Trp	Leu
1745						1750					1755			

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Met Lys Asp Thr Lys Asn Met Glu Ala Lys Lys Leu Ser Lys Asp
1760 1765 1770

Arg Met Lys Lys Tyr Met Ala Arg Arg Lys Trp Gln Lys Thr Gly
1775 1780 1785

Asn Ala Val Arg Ala Ile Gly Arg Leu Ser Ser Met Ala Met Ile
1790 1795 1800

Ser Gly Leu Ser Gly Arg Lys Ser Ser Thr Gly Ser Pro Thr Ser
1805 1810 1815

Pro Leu Asn Ala Glu Lys Leu Glu Ser Glu Glu Asp Val Ser Gln
1820 1825 1830

Ala Phe Leu Glu Ala Val Ala Glu Glu Lys Pro His Val Lys Pro
1835 1840 1845

Tyr Phe Ser Lys Thr Ile Arg Asp Leu Glu Val Val Glu Gly Ser
1850 1855 1860

Ala Ala Arg Phe Asp Cys Lys Ile Glu Gly Tyr Pro Asp Pro Glu
1865 1870 1875

Val Val Trp Phe Lys Asp Asp Gln Ser Ile Arg Glu Ser Arg His
1880 1885 1890

Phe Gln Ile Asp Tyr Asp Glu Asp Gly Asn Cys Ser Leu Ile Ile
1895 1900 1905

Ser Asp Val Cys Gly Asp Asp Asp Ala Lys Tyr Thr Cys Lys Ala
1910 1915 1920

Val Asn Ser Leu Gly Glu Ala Thr Cys Thr Ala Glu Leu Ile Val
1925 1930 1935

Glu Thr Met Glu Glu Gly Glu Gly Glu Gly Glu Glu Glu Glu Glu
1940 1945 1950

<210> 93

<211> 901

<212> PRT

<213> Homo Sapiens

<400> 93

Val Gly Arg Ala Arg Ala Pro Gly Ala Gln Val Gly Ala Gly Ala Met
1 5 10 15

Glu Pro Pro Thr Val Pro Ser Glu Arg Ser Leu Ser Leu Ser Leu Pro
20 25 30

Gly Pro Arg Glu Gly Gln Ala Thr Leu Lys Pro Pro Pro Gln His Leu
35 40 45

Trp Arg Gln Pro Arg Thr Pro Ile Arg Ile Gln Gln Arg Gly Tyr Ser
50 55 60

Asp Ser Ala Glu Arg Ala Glu Arg Glu Arg Gln Pro His Arg Pro Ile

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65					70					75				80	
Glu	Arg	Ala	Asp	Ala	Met	Asp	Thr	Ser	Asp	Arg	Pro	Gly	Leu	Arg	Thr
				85					90					95	
Thr	Arg	Met	Ser	Trp	Pro	Ser	Ser	Phe	His	Gly	Thr	Gly	Thr	Gly	Ser
			100					105					110		
Gly	Gly	Ala	Gly	Gly	Gly	Ser	Ser	Arg	Arg	Phe	Glu	Ala	Glu	Asn	Gly
		115					120					125			
Pro	Thr	Pro	Ser	Pro	Gly	Arg	Ser	Pro	Leu	Asp	Ser	Gln	Ala	Ser	Pro
	130					135					140				
Gly	Leu	Val	Leu	His	Ala	Gly	Ala	Ala	Thr	Ser	Gln	Arg	Arg	Glu	Ser
145					150					155					160
Phe	Leu	Tyr	Arg	Ser	Asp	Ser	Asp	Tyr	Asp	Met	Ser	Pro	Lys	Thr	Met
				165					170					175	
Ser	Arg	Asn	Ser	Ser	Val	Thr	Ser	Glu	Ala	His	Ala	Glu	Asp	Leu	Ile
			180					185					190		
Val	Thr	Pro	Phe	Ala	Gln	Val	Leu	Ala	Ser	Leu	Arg	Ser	Val	Arg	Ser
		195					200					205			
Asn	Phe	Ser	Leu	Leu	Thr	Asn	Val	Pro	Val	Pro	Ser	Asn	Lys	Arg	Ser
	210					215					220				
Pro	Leu	Gly	Gly	Pro	Thr	Pro	Val	Cys	Lys	Ala	Thr	Leu	Ser	Glu	Glu
225					230					235					240
Thr	Cys	Gln	Gln	Leu	Ala	Arg	Glu	Thr	Leu	Glu	Glu	Leu	Asp	Trp	Cys
				245					250					255	
Leu	Glu	Gln	Leu	Glu	Thr	Met	Gln	Thr	Tyr	Arg	Ser	Val	Ser	Glu	Met
			260					265					270		
Ala	Ser	His	Lys	Phe	Lys	Arg	Met	Leu	Asn	Arg	Glu	Leu	Thr	His	Leu
		275					280					285			
Ser	Glu	Met	Ser	Arg	Ser	Gly	Asn	Gln	Val	Ser	Glu	Tyr	Ile	Ser	Thr
	290					295					300				
Thr	Phe	Leu	Asp	Lys	Gln	Asn	Glu	Val	Glu	Ile	Pro	Ser	Pro	Thr	Met
305					310					315					320
Lys	Glu	Arg	Glu	Lys	Gln	Gln	Ala	Pro	Arg	Pro	Arg	Pro	Ser	Gln	Pro
				325					330					335	
Pro	Pro	Pro	Pro	Val	Pro	His	Leu	Gln	Pro	Met	Ser	Gln	Ile	Thr	Gly
			340					345					350		
Leu	Lys	Lys	Leu	Met	His	Ser	Asn	Ser	Leu	Asn	Asn	Ser	Asn	Ile	Pro
		355					360					365			
Arg	Phe	Gly	Val	Lys	Thr	Asp	Gln	Glu	Glu	Leu	Leu	Ala	Gln	Glu	Leu
	370					375					380				
Glu	Asn	Leu	Asn	Lys	Trp	Gly	Leu	Asn	Ile	Phe	Cys	Val	Ser	Asp	Tyr

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385		390		395		400
Ala Gly Gly Arg Ser	Leu Thr Cys Ile Met Tyr Met Ile Phe Gln Glu					
	405		410			415
Arg Asp Leu Leu Lys Lys Phe Arg Ile Pro Val Asp Thr Met Val Thr						
	420		425			430
Tyr Met Leu Thr Leu Glu Asp His Tyr His Ala Asp Val Ala Tyr His						
	435		440			445
Asn Ser Leu His Ala Ala Asp Val Leu Gln Ser Thr His Val Leu Leu						
	450		455			460
Ala Thr Pro Ala Leu Asp Ala Val Phe Thr Asp Leu Glu Ile Leu Ala						
	465		470		475	480
Ala Leu Phe Ala Ala Ala Ile His Asp Val Asp His Pro Gly Val Ser						
		485		490		495
Asn Gln Phe Leu Ile Asn Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn						
	500		505			510
Asp Glu Ser Val Leu Glu Asn His His Leu Ala Val Gly Phe Lys Leu						
	515		520			525
Leu Gln Glu Asp Asn Cys Asp Ile Phe Gln Asn Leu Ser Lys Arg Gln						
	530		535			540
Arg Gln Ser Leu Arg Lys Met Val Ile Asp Met Val Leu Ala Thr Asp						
	545		550		555	560
Met Ser Lys His Met Thr Leu Leu Ala Asp Leu Lys Thr Met Val Glu						
		565		570		575
Thr Lys Lys Val Thr Ser Ser Gly Val Leu Leu Leu Asp Asn Tyr Ser						
	580		585			590
Asp Arg Ile Gln Val Leu Arg Asn Met Val His Cys Ala Asp Leu Ser						
	595		600			605
Asn Pro Thr Lys Pro Leu Glu Leu Tyr Arg Gln Trp Thr Asp Arg Ile						
	610		615			620
Met Ala Glu Phe Phe Gln Gln Gly Asp Arg Glu Arg Glu Arg Gly Met						
	625		630		635	640
Glu Ile Ser Pro Met Cys Asp Lys His Thr Ala Ser Val Glu Lys Ser						
		645		650		655
Gln Val Gly Phe Ile Asp Tyr Ile Val His Pro Leu Trp Glu Thr Trp						
	660		665			670
Ala Asp Leu Val His Pro Asp Ala Gln Glu Ile Leu Asp Thr Leu Glu						
	675		680			685
Asp Asn Arg Asp Trp Tyr Tyr Ser Ala Ile Arg Gln Ser Pro Ser Pro						
	690		695			700
Pro Pro Glu Glu Glu Ser Arg Gly Pro Gly His Pro Pro Leu Pro Asp						

705				710				715				720			
Lys	Phe	Gln	Phe	Glu 725	Leu	Thr	Leu	Glu	Glu	Glu	Glu	Glu	Glu	Glu	Ile
Ser	Met	Ala	Gln	Ile 740	Pro	Cys	Thr	Ala	Gln	Glu	Ala	Leu	Thr	Ala	Gln
Gly	Leu	Ser	Gly	Val 755	Glu	Glu	Ala	Leu	Asp	Ala	Thr	Ile 765	Ala	Trp	Glu
Ala	Ser	Pro	Ala	Gln 770	Glu	Ser	Leu	Glu	Val	Met	Ala	Gln 780	Glu	Ala	Ser
Leu 785	Glu	Ala	Glu	Leu 790	Glu	Ala	Val	Tyr	Leu	Thr	Gln	Gln 795	Ala	Gln	Ser 800
Thr	Gly	Ser	Ala	Pro 805	Val	Ala	Pro	Asp	Glu	Phe	Ser	Ser 810	Arg	Glu	Glu
Phe	Val	Val	Ala	Val 820	Ser	His	Ser	Ser 825	Pro	Ser	Ala	Leu 830	Ala	Leu	Gln
Ser	Pro	Leu	Leu	Pro 835	Ala	Trp	Arg	Thr 840	Leu	Ser	Val	Ser 845	Glu	His	Ala
Pro	Gly	Leu	Pro	Gly 850	Leu	Pro	Ser	Thr 855	Ala	Ala	Glu	Val 860	Glu	Ala	Gln
Arg 865	Glu	His	Gln	Ala 870	Ala	Lys	Arg	Ala	Cys	Ser	Ala	Cys 875	Ala	Gly	Thr 880
Phe	Gly	Glu	Asp	Thr 885	Ser	Ala	Leu	Pro	Ala	Pro	Gly	Gly 890	Gly	Gly	Ser
Gly	Gly	Asp	Pro	Thr 900											

<400> 94

Pro	Ala	Ser	Gly	Arg	Ala	Pro	Gln	Pro	Gly	Arg	Cys	Thr	Cys	Gln	Gly
1				5					10					15	
Asn	Lys	Leu	Glu	Glu	Gln	Asp	Pro	Arg	Pro	Leu	Gln	Pro	Ile	Pro	Gly
			20					25					30		
Leu	Met	Glu	Gly	Asn	Lys	Leu	Glu	Glu	Gln	Asp	Ser	Ser	Pro	Pro	Gln
		35					40					45			
Ser	Thr	Pro	Gly	Leu	Met	Lys	Gly	Asn	Lys	Arg	Glu	Glu	Gln	Gly	Leu
	50					55					60				
Gly	Pro	Glu	Pro	Ala	Ala	Pro	Gln	Gln	Pro	Thr	Ala	Glu	Glu	Glu	Ala
65				70					75					80	

Leu	Ile	Glu	Phe	His 85	Arg	Ser	Tyr	Arg	Glu 90	Leu	Phe	Glu	Phe	Cys 95	
Asn	Asn	Thr	Thr	Ile 100	His	Gly	Ala	Ile 105	Arg	Leu	Val	Cys	Ser 110	Gln	His
Asn	Arg	Met	Lys	Thr	Ala	Phe	Trp 120	Ala	Val	Leu	Trp	Leu 125	Cys	Thr	Phe
Gly	Met 130	Met	Tyr	Trp	Gln	Phe 135	Gly	Leu	Leu	Phe	Gly 140	Glu	Tyr	Phe	Ser
Tyr 145	Pro	Val	Ser	Leu	Asn 150	Ile	Asn	Leu	Asn	Ser 155	Asp	Lys	Leu	Val	Phe 160
Pro	Ala	Val	Thr	Ile 165	Cys	Thr	Leu	Asn 170	Pro	Tyr	Arg	Tyr	Pro	Glu 175	Ile
Lys	Glu	Glu	Leu 180	Glu	Glu	Leu	Asp	Arg 185	Ile	Thr	Glu	Gln	Thr 190	Leu	Phe
Asp	Leu	Tyr 195	Lys	Tyr	Ser	Ser	Phe 200	Thr	Thr	Leu	Val	Ala 205	Gly	Ser	Arg
Ser	Arg 210	Arg	Asp	Leu	Arg	Gly 215	Thr	Leu	Pro	His 220	Pro	Leu	Gln	Arg	Leu
Arg 225	Val	Pro	Pro	Pro	Pro 230	His	Gly	Ala	Arg	Arg 235	Ala	Arg	Ser	Val	Ala 240
Ser	Ser	Leu	Arg	Asp 245	Asn	Asn	Pro	Gln	Val 250	Asp	Trp	Lys	Asp	Trp 255	Lys
Ile	Gly	Phe	Gln 260	Leu	Cys	Asn	Gln	Asn 265	Lys	Ser	Asp	Cys	Phe 270	Tyr	Gln
Thr	Tyr	Ser 275	Ser	Gly	Val	Asp	Ala 280	Val	Arg	Glu	Trp	Tyr 285	Arg	Phe	His
Tyr 290	Ile	Asn	Ile	Leu	Ser	Arg 295	Leu	Pro	Glu	Thr	Leu 300	Pro	Ser	Leu	Glu
Glu 305	Asp	Thr	Leu	Gly	Asn 310	Phe	Ile	Phe	Ala	Cys 315	Arg	Phe	Asn	Gln	Val 320
Ser	Cys	Asn	Gln	Ala 325	Asn	Tyr	Ser	His	Phe 330	His	His	Pro	Met	Tyr 335	Gly
Asn	Cys	Tyr	Thr 340	Phe	Asn	Asp	Lys	Asn 345	Asn	Ser	Asn	Leu 350	Trp	Met	Ser
Ser	Met	Pro 355	Gly	Ile	Asn	Asn	Gly 360	Leu	Ser	Leu	Met	Leu 365	Arg	Ala	Glu
Gln 370	Asn	Asp	Phe	Ile	Pro	Leu 375	Leu	Ser	Thr	Val	Thr 380	Gly	Ala	Arg	Val
Met 385	Val	His	Gly	Gln	Asp 390	Glu	Pro	Ala	Phe	Met 395	Asp	Asp	Gly	Gly	Phe 400

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Asn Leu Arg Pro Gly Val Glu Thr Ser Ile Ser Met Arg Lys Glu Thr
 405 410 415
 Leu Asp Arg Leu Gly Gly Asp Tyr Gly Asp Cys Thr Lys Asn Gly Ser
 420 425 430
 Asp Val Pro Val Glu Asn Leu Tyr Pro Ser Lys Tyr Thr Gln Gln Val
 435 440 445
 Cys Ile His Ser Cys Phe Gln Glu Ser Met Ile Lys Glu Cys Gly Cys
 450 455 460
 Ala Tyr Ile Phe Tyr Pro Arg Pro Gln Asn Val Glu Tyr Cys Asp Tyr
 465 470 475 480
 Arg Lys His Ser Ser Trp Gly Tyr Cys Tyr Tyr Lys Leu Gln Val Asp
 485 490 495
 Phe Ser Ser Asp His Leu Gly Cys Phe Thr Lys Cys Arg Lys Pro Cys
 500 505 510
 Ser Val Thr Ser Tyr Gln Leu Ser Ala Gly Tyr Ser Arg Trp Pro Ser
 515 520 525
 Val Thr Ser Gln Glu Trp Val Phe Gln Met Leu Ser Arg Gln Asn Asn
 530 535 540
 Tyr Thr Val Asn Asn Lys Arg Asn Gly Val Ala Lys Val Asn Ile Phe
 545 550 555 560
 Phe Lys Glu Leu Asn Tyr Lys Thr Asn Ser Glu Ser Pro Ser Val Thr
 565 570 575
 Met Val Thr Leu Leu Ser Asn Leu Gly Ser Gln Trp Ser Leu Trp Phe
 580 585 590
 Gly Ser Ser Val Leu Ser Val Val Glu Met Ala Glu Leu Val Phe Asp
 595 600 605
 Leu Leu Val Ile Met Phe Leu Met Leu Leu Arg Arg Phe Arg Ser Arg
 610 615 620
 Tyr Trp Ser Pro Gly Arg Gly Gly Arg Gly Ala Gln Glu Val Ala Ser
 625 630 635 640
 Thr Leu Ala Ser Ser Pro Pro Ser His Phe Cys Pro His Pro Met Ser
 645 650 655
 Leu Ser Leu Ser Gln Pro Gly Pro Ala Pro Ser Pro Ala Leu Thr Ala
 660 665 670
 Pro Pro Pro Ala Tyr Ala Thr Leu Gly Pro Arg Pro Ser Pro Gly Gly
 675 680 685
 Ser Ala Gly Ala Ser Ser Ser Thr Cys Pro Leu Gly Gly Pro
 690 695 700

<210> 95
 <211> 109
 <212> PRT

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<213> Homo Sapiens

<400> 95

Ala Tyr Ser Arg Gly Thr Ser Ser Leu Ser Thr Met Asn Gln Thr Ala
1 5 10 15

Ile Leu Ile Cys Cys Leu Ile Phe Leu Thr Leu Ser Gly Ile Gln Gly
20 25 30

Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys Ile Ser Ile Ser Asn
35 40 45

Gln Pro Val Asn Pro Arg Ser Leu Glu Lys Leu Glu Ile Ile Pro Ala
50 55 60

Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala Thr Met Lys Lys Lys
65 70 75 80

Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser Lys Ala Ile Lys Asn Leu
85 90 95

Leu Lys Ala Val Ser Lys Glu Met Ser Lys Arg Ser Pro
100 105

<210> 96

<211> 249

<212> PRT

<213> Homo Sapiens

<400> 96

Glu Phe Pro Glu Glu Ala Asn Pro Ala Gly Ile Arg Ala Ile Arg Thr
1 5 10 15

Ala Thr Met Thr Val Gly Lys Ser Ser Lys Met Leu Gln His Ile Asp
20 25 30

Tyr Arg Met Arg Cys Ile Leu Gln Asp Gly Arg Ile Phe Ile Gly Thr
35 40 45

Phe Lys Ala Phe Asp Lys His Met Asn Leu Ile Leu Cys Asp Cys Asp
50 55 60

Glu Phe Arg Lys Ile Lys Pro Lys Asn Ser Lys Gln Ala Glu Arg Glu
65 70 75 80

Glu Lys Arg Val Leu Gly Leu Val Leu Leu Arg Gly Glu Asn Leu Val
85 90 95

Ser Met Thr Val Glu Gly Pro Pro Pro Lys Asp Thr Gly Ile Ala Arg
100 105 110

Val Pro Leu Ala Gly Ala Ala Gly Gly Pro Gly Ile Gly Arg Ala Ala
115 120 125

Gly Arg Gly Ile Pro Ala Gly Val Pro Met Pro Gln Ala Pro Ala Gly
130 135 140

Leu Ala Gly Pro Val Arg Gly Val Gly Gly Pro Ser Gln Gln Val Met

145					150					155					160		
Thr	Pro	Gln	Gly	Arg	Gly	Thr	Val	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Thr		
				165					170					175			
Ala	Ser	Ile	Ala	Gly	Ala	Pro	Thr	Gln	Tyr	Pro	Pro	Gly	Arg	Gly	Gly		
				180					185					190			
Pro	Pro	Pro	Pro	Met	Gly	Arg	Gly	Ala	Pro	Pro	Pro	Gly	Met	Met	Gly		
				195					200					205			
Pro	Pro	Pro	Gly	Met	Arg	Pro	Pro	Met	Gly	Pro	Pro	Met	Gly	Ile	Pro		
				210					215					220			
Pro	Gly	Arg	Gly	Thr	Pro	Met	Gly	Met	Pro	Pro	Pro	Gly	Met	Arg	Pro		
225					230					235					240		
Pro	Pro	Pro	Gly	Met	Arg	Gly	Leu	Leu									
				245													

<400> 97

Leu 1	Leu	Leu	Trp	Leu 5	Asn	Pro	Gln	Ala	Leu 10	Val	Gly	Ala	Gln	Gly 15	Gly
Arg	Met	Ser	Gln 20	Trp	Tyr	Glu	Leu	Gln 25	Gln	Leu	Asp	Ser	Lys 30	Phe	Leu
Glu	Gln	Val 35	His	Gln	Leu	Tyr	Asp 40	Asp	Ser	Phe	Pro	Met 45	Glu	Ile	Arg
Gln	Tyr 50	Leu	Ala	Gln	Trp	Leu 55	Glu	Lys	Gln	Asp	Trp 60	Glu	His	Ala	Ala
Asn 65	Asp	Val	Ser	Phe	Ala 70	Thr	Ile	Arg	Phe	His 75	Asp	Leu	Leu	Ser	Gln 80
Leu	Asp	Asp	Gln	Tyr 85	Ser	Arg	Phe	Ser	Leu 90	Glu	Asn	Asn	Phe	Leu 95	Leu
Gln	His	Asn	Ile 100	Arg	Lys	Ser	Lys	Arg 105	Asn	Leu	Gln	Asp	Asn 110	Phe	Gln
Glu	Asp	Pro 115	Ile	Gln	Met	Ser	Met 120	Ile	Ile	Tyr	Ser	Cys 125	Leu	Lys	Glu
Glu	Arg 130	Lys	Ile	Leu	Glu	Asn 135	Ala	Gln	Arg	Phe	Asn 140	Gln	Ala	Gln	Ser
Gly 145	Asn	Ile	Gln	Ser	Thr 150	Val	Met	Leu	Asp	Lys 155	Gln	Lys	Glu	Leu	Asp 160
Ser	Lys	Val	Arg	Asn 165	Val	Lys	Asp	Lys	Val 170	Met	Cys	Ile	Glu	His 175	Glu

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Ile	Lys	Ser	Leu	Glu	Asp	Leu	Gln	Asp	Glu	Tyr	Asp	Phe	Lys	Cys	Lys		
			180					185					190				
Thr	Leu	Gln	Asn	Arg	Glu	His	Glu	Thr	Asn	Gly	Val	Ala	Lys	Ser	Asp		
		195					200					205					
Gln	Lys	Gln	Glu	Gln	Leu	Leu	Leu	Lys	Lys	Met	Tyr	Leu	Met	Leu	Asp		
	210					215					220						
Asn	Lys	Arg	Lys	Glu	Val	Val	His	Lys	Ile	Ile	Glu	Leu	Leu	Asn	Val		
225					230				235						240		
Thr	Glu	Leu	Thr	Gln	Asn	Ala	Leu	Ile	Asn	Asp	Glu	Leu	Val	Glu	Trp		
				245					250					255			
Lys	Arg	Arg	Gln	Gln	Ser	Ala	Cys	Ile	Gly	Gly	Pro	Pro	Asn	Ala	Cys		
			260					265					270				
Leu	Asp	Gln	Leu	Gln	Asn	Trp	Phe	Thr	Ile	Val	Ala	Glu	Ser	Leu	Gln		
	275						280					285					
Gln	Val	Arg	Gln	Gln	Leu	Lys	Lys	Leu	Glu	Glu	Leu	Glu	Gln	Lys	Tyr		
	290					295					300						
Thr	Tyr	Glu	His	Asp	Pro	Ile	Thr	Lys	Asn	Lys	Gln	Val	Leu	Trp	Asp		
305					310					315					320		
Arg	Thr	Phe	Ser	Leu	Phe	Gln	Gln	Leu	Ile	Gln	Ser	Ser	Phe	Val	Val		
				325					330					335			
Glu	Arg	Gln	Pro	Cys	Met	Pro	Thr	His	Pro	Gln	Arg	Pro	Leu	Val	Leu		
			340					345					350				
Lys	Thr	Gly	Val	Gln	Phe	Thr	Val	Lys	Leu	Arg	Leu	Leu	Val	Lys	Leu		
		355					360					365					
Gln	Glu	Leu	Asn	Tyr	Asn	Leu	Lys	Val	Lys	Val	Leu	Phe	Asp	Lys	Asp		
	370					375					380						
Val	Asn	Glu	Arg	Asn	Thr	Val	Lys	Gly	Phe	Arg	Lys	Phe	Asn	Ile	Leu		
385					390				395						400		
Gly	Thr	His	Thr	Lys	Val	Met	Asn	Met	Glu	Glu	Ser	Thr	Asn	Gly	Ser		
				405					410					415			
Leu	Ala	Ala	Glu	Phe	Arg	His	Leu	Gln	Leu	Lys	Glu	Gln	Lys	Asn	Ala		
			420					425					430				
Gly	Thr	Arg	Thr	Asn	Glu	Gly	Pro	Leu	Ile	Val	Thr	Glu	Glu	Leu	His		
		435					440					445					
Ser	Leu	Ser	Phe	Glu	Thr	Gln	Leu	Cys	Gln	Pro	Gly	Leu	Val	Ile	Asp		
	450					455					460						
Leu	Glu	Thr	Thr	Ser	Leu	Pro	Val	Val	Val	Ile	Ser	Asn	Val	Ser	Gln		
465					470					475					480		
Leu	Pro	Ser	Gly	Trp	Ala	Ser	Ile	Leu	Trp	Tyr	Asn	Met	Leu	Val	Ala		
				485					490					495			

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Glu Pro Arg Asn Leu Ser Phe Phe Leu Thr Pro Pro Cys Ala Arg Trp
 500 505 510
 Ala Gln Leu Ser Glu Val Leu Ser Trp Gln Phe Ser Ser Val Thr Lys
 515 520 525
 Arg Gly Leu Asn Val Asp Gln Leu Asn Met Leu Gly Glu Lys Leu Leu
 530 535 540
 Gly Pro Asn Ala Ser Pro Asp Gly Leu Ile Pro Trp Thr Arg Phe Cys
 545 550 555 560
 Lys Glu Asn Ile Asn Asp Lys Asn Phe Pro Phe Trp Leu Trp Ile Glu
 565 570 575
 Ser Ile Leu Glu Leu Ile Lys Lys His Leu Leu Pro Leu Trp Asn Asp
 580 585 590
 Gly Cys Ile Met Gly Phe Ile Ser Lys Glu Arg Glu Arg Ala Leu Leu
 595 600 605
 Lys Asp Gln Gln Pro Gly Thr Phe Leu Leu Arg Phe Ser Glu Ser Ser
 610 615 620
 Arg Glu Gly Ala Ile Thr Phe Thr Trp Val Glu Arg Ser Gln Asn Gly
 625 630 635 640
 Gly Glu Pro Asp Phe His Ala Val Glu Pro Tyr Thr Lys Lys Glu Leu
 645 650 655
 Ser Ala Val Thr Phe Pro Asp Ile Ile Arg Asn Tyr Lys Val Met Ala
 660 665 670
 Ala Glu Asn Ile Pro Glu Asn Pro Leu Lys Tyr Leu Tyr Pro Asn Ile
 675 680 685
 Asp Lys Asp His Ala Phe Gly Lys Tyr Tyr Ser Arg Pro Lys Glu Ala
 690 695 700
 Pro Glu Pro Met Glu Leu Asp Gly Pro Lys Gly Thr Gly Tyr Ile Lys
 705 710 715 720
 Thr Glu Leu Ile Ser Val Ser Glu Val
 725

<210> 98
 <211> 1575
 <212> PRT
 <213> Homo Sapiens

<400> 98

Arg Gly Arg Leu Leu Gly Leu Leu Asn Pro Ser Val Ser Leu Gly Arg
 1 5 10 15
 Pro Lys Val Arg Val Met Tyr Arg Asp Glu Cys Lys Lys His Leu Ala
 20 25 30
 Gly Leu Gly Ala Leu Gly Leu Gly Ser Leu Ile Thr Glu Leu Thr Ala
 35 40 45

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Asn	Glu	Glu	Leu	Thr	Gly	Thr	Asp	Gly	Ala	Leu	Val	Asn	Asp	Glu	Gly	50	55	60	
Trp	Val	Arg	Ser	Thr	Glu	Asp	Ala	Val	Asp	Tyr	Ser	Asp	Ile	Asn	Glu	65	70	75	80
Val	Ala	Glu	Asp	Glu	Ser	Arg	Arg	Tyr	Gln	Gln	Thr	Met	Gly	Ser	Leu	85	90	95	
Gln	Pro	Leu	Cys	His	Ser	Asp	Tyr	Asp	Glu	Asp	Asp	Tyr	Asp	Ala	Asp	100	105	110	
Cys	Glu	Asp	Ile	Asp	Cys	Lys	Leu	Met	Pro	Pro	Pro	Pro	Pro	Pro	Pro	115	120	125	
Gly	Pro	Met	Lys	Lys	Asp	Lys	Asp	Gln	Asp	Ser	Ile	Thr	Gly	Glu	Lys	130	135	140	
Val	Asp	Phe	Ser	Ser	Ser	Ser	Asp	Ser	Glu	Ser	Glu	Met	Gly	Pro	Gln	145	150	155	160
Glu	Ala	Thr	Gln	Ala	Glu	Ser	Glu	Asp	Gly	Lys	Leu	Thr	Leu	Pro	Leu	165	170	175	
Ala	Gly	Ile	Met	Gln	His	Asp	Ala	Thr	Lys	Leu	Leu	Pro	Ser	Val	Thr	180	185	190	
Glu	Leu	Phe	Pro	Glu	Phe	Arg	Pro	Gly	Lys	Val	Leu	Arg	Phe	Leu	Arg	195	200	205	
Leu	Phe	Gly	Pro	Gly	Lys	Asn	Val	Pro	Ser	Val	Trp	Arg	Ser	Ala	Arg	210	215	220	
Arg	Lys	Arg	Lys	Lys	Lys	His	Arg	Glu	Leu	Ile	Gln	Glu	Glu	Gln	Ile	225	230	235	240
Gln	Glu	Val	Glu	Cys	Ser	Val	Glu	Ser	Glu	Val	Ser	Gln	Lys	Ser	Leu	245	250	255	
Trp	Asn	Tyr	Asp	Tyr	Ala	Pro	Pro	Pro	Pro	Pro	Glu	Gln	Cys	Leu	Ser	260	265	270	
Asp	Asp	Glu	Ile	Thr	Met	Met	Ala	Pro	Val	Glu	Ser	Lys	Phe	Ser	Gln	275	280	285	
Ser	Thr	Gly	Asp	Ile	Asp	Lys	Val	Thr	Asp	Thr	Lys	Pro	Arg	Val	Ala	290	295	300	
Glu	Trp	Arg	Tyr	Gly	Pro	Ala	Arg	Leu	Trp	Tyr	Asp	Met	Leu	Gly	Val	305	310	315	320
Pro	Glu	Asp	Gly	Ser	Gly	Phe	Asp	Tyr	Gly	Phe	Lys	Leu	Arg	Lys	Thr	325	330	335	
Glu	His	Glu	Pro	Val	Ile	Lys	Ser	Arg	Met	Ile	Glu	Glu	Phe	Arg	Lys	340	345	350	
Leu	Glu	Glu	Asn	Asn	Gly	Thr	Asp	Leu	Leu	Ala	Asp	Glu	Asn	Phe	Leu	355	360	365	

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Met	Val	Thr	Gln	Leu	His	Trp	Glu	Asp	Asp	Ile	Ile	Trp	Asp	Gly	Glu	370	375	380
Asp	Val	Lys	His	Lys	Gly	Thr	Lys	Pro	Gln	Arg	Ala	Ser	Leu	Ala	Gly	385	390	395
Trp	Leu	Pro	Ser	Ser	Met	Thr	Arg	Asn	Ala	Met	Ala	Tyr	Asn	Val	Gln	405	410	415
Gln	Gly	Phe	Ala	Ala	Thr	Leu	Asp	Asp	Asp	Lys	Pro	Trp	Tyr	Ser	Ile	420	425	430
Phe	Pro	Ile	Asp	Asn	Glu	Asp	Leu	Val	Tyr	Gly	Arg	Trp	Glu	Asp	Asn	435	440	445
Ile	Ile	Trp	Asp	Ala	Gln	Ala	Met	Pro	Arg	Leu	Leu	Glu	Pro	Pro	Val	450	455	460
Leu	Thr	Leu	Asp	Pro	Asn	Asp	Glu	Asn	Leu	Ile	Leu	Glu	Ile	Pro	Asp	465	470	475
Glu	Lys	Glu	Glu	Ala	Thr	Ser	Asn	Ser	Pro	Ser	Lys	Glu	Ser	Lys	Lys	485	490	495
Glu	Ser	Ser	Leu	Lys	Lys	Ser	Arg	Ile	Leu	Leu	Gly	Lys	Thr	Gly	Val	500	505	510
Ile	Lys	Glu	Glu	Pro	Gln	Gln	Asn	Met	Ser	Gln	Pro	Glu	Val	Lys	Asp	515	520	525
Pro	Trp	Asn	Leu	Ser	Asn	Asp	Glu	Tyr	Tyr	Tyr	Pro	Lys	Gln	Gln	Gly	530	535	540
Leu	Arg	Gly	Thr	Phe	Gly	Gly	Asn	Ile	Ile	Gln	His	Ser	Ile	Pro	Ala	545	550	555
Val	Glu	Leu	Arg	Gln	Pro	Phe	Phe	Pro	Thr	His	Met	Gly	Pro	Ile	Lys	565	570	575
Leu	Arg	Gln	Phe	His	Arg	Pro	Pro	Leu	Lys	Lys	Tyr	Ser	Phe	Gly	Ala	580	585	590
Leu	Ser	Gln	Pro	Gly	Pro	His	Ser	Val	Gln	Pro	Leu	Leu	Lys	His	Ile	595	600	605
Lys	Lys	Lys	Ala	Lys	Met	Arg	Glu	Gln	Glu	Arg	Gln	Ala	Ser	Gly	Gly	610	615	620
Gly	Glu	Met	Phe	Phe	Met	Arg	Thr	Pro	Gln	Asp	Leu	Thr	Gly	Lys	Asp	625	630	635
Gly	Asp	Leu	Ile	Leu	Ala	Glu	Tyr	Ser	Glu	Glu	Asn	Gly	Pro	Leu	Met	645	650	655
Met	Gln	Val	Gly	Met	Ala	Thr	Lys	Ile	Lys	Asn	Tyr	Tyr	Lys	Arg	Lys	660	665	670
Pro	Gly	Lys	Asp	Pro	Gly	Ala	Pro	Asp	Cys	Lys	Tyr	Gly	Glu	Thr	Val	675	680	685

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Tyr Cys His Thr Ser Pro Phe Leu Gly Ser Leu His Pro Gly Gln Leu
 690 695 700
 Leu Gln Ala Phe Glu Asn Asn Leu Phe Arg Ala Pro Ile Tyr Leu His
 705 710 715 720
 Lys Met Pro Glu Thr Asp Phe Leu Ile Ile Arg Thr Arg Gln Gly Tyr
 725 730 735
 Tyr Ile Arg Glu Leu Val Asp Ile Phe Val Val Gly Gln Gln Cys Pro
 740 745 750
 Leu Phe Glu Val Pro Gly Pro Asn Ser Lys Arg Ala Asn Thr His Ile
 755 760 765
 Arg Asp Phe Leu Gln Val Phe Ile Tyr Arg Leu Phe Trp Lys Ser Lys
 770 775 780
 Asp Arg Pro Arg Arg Ile Arg Met Glu Asp Ile Lys Lys Ala Phe Pro
 785 790 795 800
 Ser His Ser Glu Ser Ser Ile Arg Lys Arg Leu Lys Leu Cys Ala Asp
 805 810 815
 Phe Lys Arg Thr Gly Met Asp Ser Asn Trp Trp Val Leu Lys Ser Asp
 820 825 830
 Phe Arg Leu Pro Thr Glu Glu Glu Ile Arg Ala Met Val Ser Pro Glu
 835 840 845
 Gln Cys Cys Ala Tyr Tyr Ser Met Ile Ala Ala Glu Gln Arg Leu Lys
 850 855 860
 Asp Ala Gly Tyr Gly Glu Lys Ser Phe Phe Ala Pro Glu Glu Glu Asn
 865 870 875 880
 Glu Glu Asp Phe Gln Met Lys Ile Asp Asp Glu Val Arg Thr Ala Pro
 885 890 895
 Trp Asn Thr Thr Arg Ala Phe Ile Ala Ala Met Lys Gly Lys Cys Leu
 900 905 910
 Leu Glu Val Thr Gly Val Ala Asp Pro Thr Gly Cys Gly Glu Gly Phe
 915 920 925
 Ser Tyr Val Lys Ile Pro Asn Lys Pro Thr Gln Gln Lys Asp Asp Lys
 930 935 940
 Glu Pro Gln Pro Val Lys Lys Thr Val Thr Gly Thr Asp Ala Asp Leu
 945 950 955 960
 Arg Arg Leu Ser Leu Lys Asn Ala Lys Gln Leu Leu Arg Lys Phe Gly
 965 970 975
 Val Pro Glu Glu Glu Ile Lys Lys Leu Ser Arg Trp Glu Val Ile Asp
 980 985 990
 Val Val Arg Thr Met Ser Thr Glu Gln Ala Arg Ser Gly Glu Gly Pro
 995 1000 1005

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Met	Ser	Lys	Phe	Ala	Arg	Gly	Ser	Arg	Phe	Ser	Val	Ala	Glu	His
1010						1015					1020			
Gln	Glu	Arg	Tyr	Lys	Glu	Glu	Cys	Gln	Arg	Ile	Phe	Asp	Leu	Gln
1025						1030					1035			
Asn	Lys	Val	Leu	Ser	Ser	Thr	Glu	Val	Leu	Ser	Thr	Asp	Thr	Asp
1040						1045					1050			
Ser	Ser	Ser	Ala	Glu	Asp	Ser	Asp	Phe	Glu	Glu	Met	Gly	Lys	Asn
1055						1060					1065			
Ile	Glu	Asn	Met	Leu	Gln	Asn	Lys	Lys	Thr	Ser	Ser	Gln	Leu	Ser
1070						1075					1080			
Arg	Glu	Arg	Glu	Glu	Gln	Glu	Arg	Lys	Glu	Leu	Gln	Arg	Met	Leu
1085						1090					1095			
Leu	Ala	Ala	Gly	Ser	Ala	Ala	Ser	Gly	Asn	Asn	His	Arg	Asp	Asp
1100						1105					1110			
Asp	Thr	Ala	Ser	Val	Thr	Ser	Leu	Asn	Ser	Ser	Ala	Thr	Gly	Arg
1115						1120					1125			
Cys	Leu	Lys	Ile	Tyr	Arg	Thr	Phe	Arg	Asp	Glu	Glu	Gly	Lys	Glu
1130						1135					1140			
Tyr	Val	Arg	Cys	Glu	Thr	Val	Arg	Lys	Pro	Ala	Val	Ile	Asp	Ala
1145						1150					1155			
Tyr	Val	Arg	Ile	Arg	Thr	Thr	Lys	Asp	Glu	Glu	Phe	Ile	Arg	Lys
1160						1165					1170			
Phe	Ala	Leu	Phe	Asp	Glu	Gln	His	Arg	Glu	Glu	Met	Arg	Lys	Glu
1175						1180					1185			
Arg	Arg	Arg	Ile	Gln	Glu	Gln	Leu	Arg	Arg	Leu	Lys	Arg	Asn	Gln
1190						1195					1200			
Glu	Lys	Glu	Lys	Leu	Lys	Gly	Pro	Pro	Glu	Lys	Lys	Pro	Lys	Lys
1205						1210					1215			
Met	Lys	Glu	Arg	Pro	Asp	Leu	Lys	Leu	Lys	Cys	Gly	Ala	Cys	Gly
1220						1225					1230			
Ala	Ile	Gly	His	Met	Arg	Thr	Asn	Lys	Phe	Cys	Pro	Leu	Tyr	Tyr
1235						1240					1245			
Gln	Thr	Asn	Ala	Pro	Pro	Ser	Asn	Pro	Val	Ala	Met	Thr	Glu	Glu
1250						1255					1260			
Gln	Glu	Glu	Glu	Leu	Glu	Lys	Thr	Val	Ile	His	Asn	Asp	Asn	Glu
1265						1270					1275			
Glu	Leu	Ile	Lys	Val	Glu	Gly	Thr	Lys	Ile	Val	Leu	Gly	Lys	Gln
1280						1285					1290			
Leu	Ile	Glu	Ser	Ala	Asp	Glu	Val	Arg	Arg	Lys	Ser	Leu	Val	Leu
1295						1300					1305			

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Lys Phe Pro Lys Gln Gln Leu Pro Pro Lys Lys Lys Arg Arg Val
 1310 1315 1320
 Gly Thr Thr Val His Cys Asp Tyr Leu Asn Arg Pro His Lys Ser
 1325 1330 1335
 Ile His Arg Arg Arg Thr Asp Pro Met Val Thr Leu Ser Ser Ile
 1340 1345 1350
 Leu Glu Ser Ile Ile Asn Asp Met Arg Asp Leu Pro Asn Thr Tyr
 1355 1360 1365
 Pro Phe His Thr Pro Val Asn Ala Lys Val Val Lys Asp Tyr Tyr
 1370 1375 1380
 Lys Ile Ile Thr Arg Pro Met Asp Leu Gln Thr Leu Arg Glu Asn
 1385 1390 1395
 Val Arg Lys Arg Leu Tyr Pro Ser Arg Glu Glu Phe Arg Glu His
 1400 1405 1410
 Leu Glu Leu Ile Val Lys Asn Ser Ala Thr Tyr Asn Gly Pro Lys
 1415 1420 1425
 His Ser Leu Thr Gln Ile Ser Gln Ser Met Leu Asp Leu Cys Asp
 1430 1435 1440
 Glu Lys Leu Lys Glu Lys Glu Asp Lys Leu Ala Arg Leu Glu Lys
 1445 1450 1455
 Ala Ile Asn Pro Leu Leu Asp Asp Asp Asp Gln Val Ala Phe Ser
 1460 1465 1470
 Phe Ile Leu Asp Asn Ile Val Thr Gln Lys Met Met Ala Val Pro
 1475 1480 1485
 Asp Ser Trp Pro Phe His His Pro Val Asn Lys Lys Phe Val Pro
 1490 1495 1500
 Asp Tyr Tyr Lys Val Ile Val Asn Pro Met Asp Leu Glu Thr Ile
 1505 1510 1515
 Arg Lys Asn Ile Ser Lys His Lys Tyr Gln Ser Arg Glu Ser Phe
 1520 1525 1530
 Leu Asp Asp Val Asn Leu Ile Leu Ala Asn Ser Val Lys Tyr Asn
 1535 1540 1545
 Asp Asn Glu Cys Ser Ser Lys Ala Asn Asp Ile Val Cys Leu Ile
 1550 1555 1560
 Gln Tyr Cys Ser Ser Gln Ile Glu Glu Leu Arg Phe
 1565 1570 1575

<210> 99
 <211> 166
 <212> PRT
 <213> Homo Sapiens

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<400> 99

Leu Cys Leu Lys Lys Lys Ile Pro Asn Met Asp Lys Pro Arg Lys Glu
 1 5 10 15
 Asn Glu Glu Glu Pro Gln Ser Arg Pro Arg Pro Met Arg Arg Gly Leu
 20 25 30
 Arg Trp Ser Thr Leu Pro Lys Ser Ser Pro Pro Arg Ser Ser Leu Arg
 35 40 45
 Arg Ser Ser Pro Arg Arg Arg Ser Ser Phe Leu Arg Ser Ser Cys Leu
 50 55 60
 Ser Ser Cys Leu Arg Cys Ser Ser Arg Arg Thr Pro Ser Ala Gly Leu
 65 70 75 80
 Ser Arg Lys Asp Leu Phe Glu Val Arg Pro Pro Met Glu Gln Pro Pro
 85 90 95
 Cys Gly Val Gly Lys His Asn Leu Glu Glu Gly Ile Phe Lys Glu Arg
 100 105 110
 Leu Ala Arg Ser Arg Pro Gln Phe Arg Gly Asp Ile His Gly Arg Asn
 115 120 125
 Leu Ser Asn Glu Glu Met Ile Gln Ala Ala Asp Glu Leu Glu Glu Met
 130 135 140
 Lys Arg Val Arg Asn Lys Leu Met Ile Met His Trp Arg Ala Lys Arg
 145 150 155 160
 Gly Gly Pro Tyr Pro Ile
 165

<210> 100

<211> 245

<212> PRT

<213> Homo Sapiens

<400> 100

Thr Lys Met Leu Lys Ser Trp Arg Ser Gly Arg Gln Ile Thr Gln Lys
 1 5 10 15
 Gly Thr Glu Asp Glu Leu Asp Lys Tyr Ser Glu Ala Leu Lys Asp Ala
 20 25 30
 Gln Glu Lys Leu Glu Leu Ala Glu Lys Lys Ala Thr Asp Ala Glu Ala
 35 40 45
 Asp Val Ala Ser Leu Asn Arg Arg Ile Gln Leu Val Glu Glu Glu Leu
 50 55 60
 Asp Arg Ala Gln Glu Arg Leu Ala Thr Ala Leu Gln Lys Leu Glu Glu
 65 70 75 80
 Ala Glu Lys Ala Ala Asp Glu Ser Glu Arg Gly Met Lys Val Ile Glu
 85 90 95

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Ser Arg Ala Gln Lys Asp Glu Glu Lys Met Glu Ile Gln Glu Ile Gln
 100 105 110

Leu Lys Glu Ala Lys His Ile Ala Glu Asp Ala Asp Arg Lys Tyr Glu
 115 120 125

Glu Val Ala Arg Lys Leu Val Ile Ile Glu Ser Asp Leu Glu Arg Ala
 130 135 140

Glu Glu Arg Ala Glu Leu Ser Glu Gly Gln Val Arg Gln Leu Glu Glu
 145 150 155 160

Gln Leu Arg Ile Met Asp Gln Thr Leu Lys Ala Leu Met Ala Ala Glu
 165 170 175

Asp Lys Tyr Ser Gln Lys Glu Asp Arg Tyr Glu Glu Glu Ile Lys Val
 180 185 190

Leu Ser Asp Lys Leu Lys Glu Ala Glu Thr Arg Ala Glu Phe Ala Glu
 195 200 205

Arg Ser Val Thr Lys Leu Glu Lys Ser Ile Asp Asp Leu Glu Glu Lys
 210 215 220

Val Leu Met Pro Lys Lys Lys Thr Leu Val Cys Ile Arg Cys Trp Ile
 225 230 235 240

Arg Leu Tyr Trp Ser
 245

<210> 101

<211> 267

<212> PRT

<213> Homo Sapiens

<400> 101

Leu Pro Val Leu Ala Ser Arg Ala Tyr Ala Ala Pro Ala Pro Gly Gln
 1 5 10 15

Ala Leu Gln Arg Val Gly Ile Val Gly Gly Gln Glu Ala Pro Arg Ser
 20 25 30

Lys Trp Pro Trp Gln Val Ser Leu Arg Val Arg Asp Arg Tyr Trp Met
 35 40 45

His Phe Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala
 50 55 60

Ala His Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val
 65 70 75 80

Gln Leu Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val
 85 90 95

Ser Arg Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala
 100 105 110

Asp Ile Ala Leu Leu Glu Leu Glu Glu Pro Val Lys Val Ser Ser His
 115 120 125

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Val His Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly
 130 135 140

Met Pro Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg
 145 150 155 160

Leu Pro Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu
 165 170 175

Asn His Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp
 180 185 190

Asp Val Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg
 195 200 205

Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val
 210 215 220

Asn Gly Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys
 225 230 235 240

Ala Gln Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu
 245 250 255

Asp Trp Ile His His Tyr Val Pro Lys Lys Pro
 260 265

<210> 102

<211> 192

<212> PRT

<213> Homo Sapiens

<400> 102

Ala Arg Ala Ser Ser Cys Leu Ser Ala Asn Ala Ala Arg Met Ala Ser
 1 5 10 15

Gln Asn Arg Asp Pro Ala Ala Thr Ser Val Ala Ala Ala Arg Lys Gly
 20 25 30

Ala Glu Pro Ser Gly Gly Ala Ala Arg Gly Pro Val Gly Lys Arg Leu
 35 40 45

Gln Gln Glu Leu Met Thr Leu Met Met Ser Gly Asp Lys Gly Ile Ser
 50 55 60

Ala Phe Pro Glu Ser Asp Asn Leu Phe Lys Trp Val Gly Thr Ile His
 65 70 75 80

Gly Ala Ala Gly Thr Val Tyr Glu Asp Leu Arg Tyr Lys Leu Ser Leu
 85 90 95

Glu Phe Pro Ser Gly Tyr Pro Tyr Asn Ala Pro Thr Val Lys Phe Leu
 100 105 110

Thr Pro Cys Tyr His Pro Asn Val Asp Thr Gln Gly Asn Ile Cys Leu
 115 120 125

Asp Ile Leu Lys Glu Lys Trp Ser Ala Leu Tyr Asp Val Arg Thr Ile

130						135						140					
Leu	Leu	Ser	Ile	Gln	Ser	Leu	Leu	Gly	Glu	Pro	Asn	Ile	Asp	Ser	Pro		
145					150					155					160		
Leu	Asn	Thr	His	Ala	Ala	Glu	Leu	Trp	Lys	Asn	Pro	Thr	Ala	Phe	Lys		
				165					170					175			
Lys	Tyr	Leu	Gln	Glu	Thr	Tyr	Ser	Lys	Gln	Val	Thr	Ser	Gln	Glu	Pro		
			180					185					190				